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CONTENTS

Prevention of retinal venous occlusion ..... *Bertha A. Klien* 175
Gonioscopic observations of iridocyclitis ..... *J. François* 185
Present status of trachoma ..... *Max Hirschfelder* 188
Keratoconjunctivitis sicca ..... *John W. Henderson* 197
Polysaccharides in ocular tissue ..... *Robert Day* 224
Megalopapilla ..... *A. Franceschetti and R. H. Bock* 227
The psychology of the poor reader ..... *William H. Crisp* 235
Studies of the eye in old age ..... *A. L. Kornzweig and Morris Feldstein* 243
Hole in the macula ..... *Leo J. Croll and Maurice Croll* 248
Cholinesterase in ocular tissues ..... *George B. Koelle and Jonas S. Friedenwald* 253
Studies on ascorbic acid ..... *V. Everett Kinsey* 257
Cytochrome-C content of lens ..... *Laurence O. Ely and W. A. Robbie* 269
Aureomycin in ophthalmology ..... *John G. Bellows, Viola M. Richardson, and Chester J. Farmer* 273
Enucleation and allied procedures ..... *Jack S. Guyton* 283
Anterior-segment photography ..... *Nicholas Douvas and Lee Allen* 291
Electronic tonometer ..... *Paul Tower* 292
Removal of rust ring of cornea ..... *Erwin E. Grossmann* 293

DEPARTMENTS

Society Proceedings 295
Editorials 301
Correspondence 303
Book Reviews 304
Abstracts 307
Pan-American Notes 339
News Items 340

For complete table of contents see advertising page xi.

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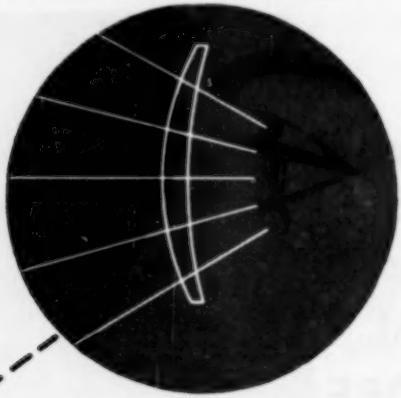

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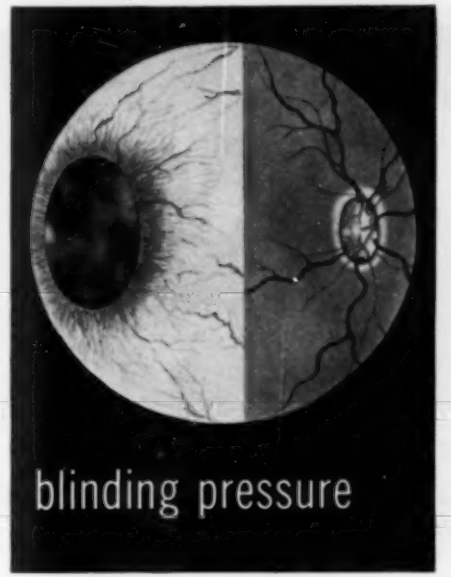

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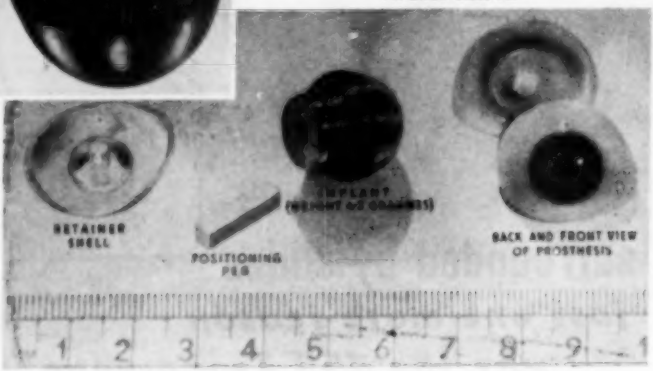

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SERIES 3 · VOLUME 33 · NUMBER 2 · FEBRUARY, 1950

CONTENTS

Color plate illustrating article by J. François. Facing 186

ORIGINAL ARTICLES

Prevention of retinal venous occlusion: With special reference to ambulatory dicumarol therapy. Bertha A. Klien 175
Gonioscopic observations during the evolution of an acute iridocyclitis. J. François 185
The present status in the treatment and prevention of trachoma. Max Hirschfelder 188
Keratoconjunctivitis sicca: A review with a survey of 121 additional cases. John W. Henderson 197
Polysaccharides in ocular tissue. Robert Day 224
Megalopapilla: A new congenital anomaly. A. Franceschetti and R. H. Bock 227
The psychology of the poor reader. William H. Crisp 235
Studies of the eye in old age: II. Hole in the macula: A clinico-pathologic study. A. L. Kornzweig and Morris Feldstein 243
Hole in the macula. Leo J. Croll and Maurice Croll 248
The histochemical localization of cholinesterase in ocular tissues. George B. Koelle and Jonas S. Friedenwald 253
Dehydroascorbic acid—Ascorbic acid in the aqueous humor of rabbits. V. Everett Kinsey 257
The cyanide sensitivity and cytochrome-C content of the crystalline lens. Lawrence O. Ely and W. A. Robbie 269
Aureomycin in ophthalmology. John G. Bellows, Viola M. Richardson, and Chester J. Farmer 273
Enucleation and allied procedures: Part III. A new procedure involving use of an "exoplant." Jack S. Guyton 283

NOTES, CASES, INSTRUMENTS

Anterior-segment photography. Nicholas Douvas and Lee Allen 291
Device for stabilizing the electronic tonometer during calibration. Paul Tower 292
Instrument for removal of rust ring of cornea. Erwin E. Grossmann 293

SOCIETY PROCEEDINGS

College of Physicians of Philadelphia, Section on Ophthalmology, February 17, 1949 295
New York Society for Clinical Ophthalmology, February 7, 1949 296
Colorado Ophthalmological Society, November 20, 1948 298

EDITORIALS

Professor Hjalmar August Schiøtz 301
The Academy's Symposia 303

CORRESPONDENCE

Charting visual fields 303
A simple aid in prescribing bifocals 304

BOOK REVIEWS

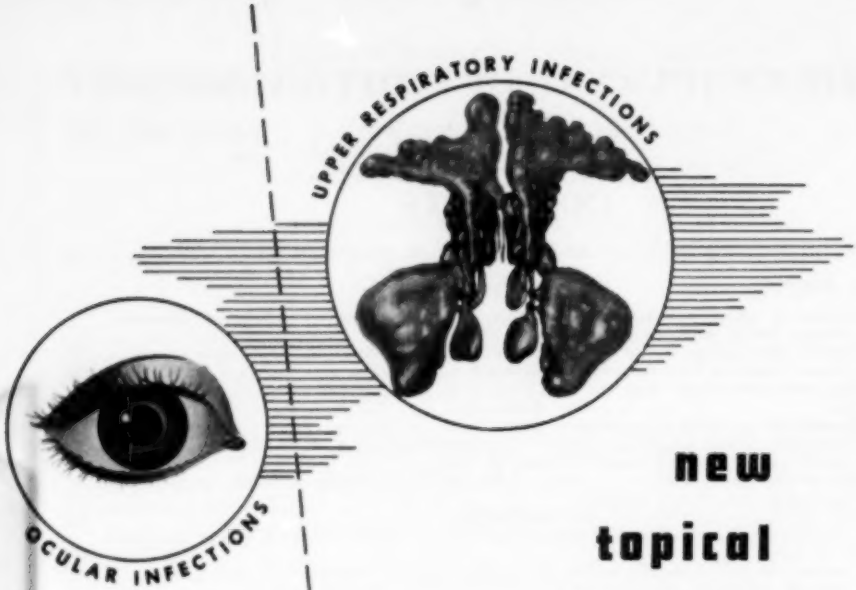
The Eye and Its Diseases 304
Practical Orthoptics in the Treatment of Squint 305
May's Manual of Diseases of the Eye 306
Microphthalmos and Anophthalmos With or Without Coincident Oligophrenia 306
The Physiology of Thought 306

ABSTRACTS

Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera; Uvea, sympathetic disease, aqueous; Glaucoma and ocular tension; Crystalline lens; Retina and vitreous; Optic nerve and chiasm; Neuro-ophthalmology; Eyeball, orbit, sinuses; Eyelids, lacrimal apparatus; Tumors; Injuries; Systemic disease and parasites; Congenital deformities, heredity; Hygiene, sociology, education, and history 307

PAN-AMERICAN NOTES 339

NEWS ITEMS 340



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AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 33 FEBRUARY, 1950 NUMBER 2

PREVENTION OF RETINAL VENOUS OCCLUSION*

WITH SPECIAL REFERENCE TO AMBULATORY DICUMAROL THERAPY

BERTHA A. KLIEN, M.D.
Chicago, Illinois

Prevention of complications of vascular disease, such as are represented by certain types of retinal venous occlusion, calls for two safeguards: (1) Recognition of the danger signals at the earliest possible time, and (2) familiarity with variations in physiologic conditions, which tend to favor or accelerate its development, should they coexist with certain pathologic processes in the course of predisposing systemic diseases such as diabetes, blood dyscrasias, the sclerotic phase of essential hypertension, spastic hypertension, and senile angiosclerosis.

The pathogenesis of the various types of venous occlusion and its bearing upon success or failure of anticoagulant therapy has been discussed in detail elsewhere (Klien[1,2]). Briefly, and quite generally speaking, the types of venous occlusion which promise the most favorable results from this therapy are those which arise from a combination of two different pathologic factors; that is, a certain amount of narrowing of the venous lumen with an abnormal readiness for thrombus formation.

A combination of the predisposing factors incidental to various systemic disorders, of increased blood volume, high viscosity, slowing of the blood flow, easy coagulability of the blood, with otherwise negligible alterations of the venous wall or a slight narrowing of the venous lumen by sclerosed adjacent structures, together with occasionally preëxisting unfavorable anatomic relations, may give rise to primary thrombus formation, leading to a type of occlusion benefited by anticoagulants.

On the other hand, advancing obliterating sclerosis alone results in the kind of occlusion in which anticoagulant therapy is of little or no value after the completed event, as thrombus formation is only the terminal step, bringing about complete obliteration of an already slitlike venous aperture. Sufficient delay of this final event to permit establishment of an efficient collateral circulation, if such is feasible at all, holds the only promise for preservation of vision, and can be attained in many cases by prompt and prolonged administration of dicumarol after the first signs of venous circulatory impairment have become manifest.

Preventive anticoagulant treatment, therefore, has a wider scope of usefulness than the curative attempts, which are made after an already accomplished occlusion.

SIGNALS OF IMMINENT RETINAL VENOUS OCCLUSION

While arterial occlusion is usually sudden and unpredictable, the development of retinal venous occlusion is, on the contrary, almost always very gradual, leading to definite, but often unrecognized, premonitory signs.

The danger signals of imminent retinal venous occlusion may be divided into subjective and objective symptoms:

* From the Department of Ophthalmology, Northwestern University Medical School, April, 1949.

The subjective symptoms are intermittent visual obscurations or a slight constant reduction of the central visual acuity, from a previous 1.2, for instance, to 1.0 or 0.8, for which no apparent reason can be found. Complaints of fullness in the head or intermittent drowsiness are not rare during this phase.

These visual disturbances may result from impairment of the circulation in the central vein, or in one of its main tributaries near their junction, or in a smaller branch in the superior macular region. Their cause is obviously collateral edema which at first is of greatly variable degree and of transient character. Along the central vein or the deep-lying junction of its immediate tributaries this edema, confined by the optic nerve and the cribriform plate, may exert pressure upon the papillomacular bundle, thereby causing a visual disturbance. In the early stages of this process, the edema may not be within the range of ophthalmoscopic visibility, but the visual obscurations, as one finds out only too often in retrospect, may precede occlusion of the central vein or a major branch by many weeks or months.

The retinal edema along an embarrassed venous branch in the superior macular region may be faintly visible if recent, but usually gravitates downward, involving directly, if only slightly, the foveolar region. Depending upon the degree of impairment of the venous flow in such a branch, the resulting slight diminution of vision will be intermittent or constant, but it may herald the occlusion many months ahead of the actual event. Occasionally a paracentral scotoma can be demonstrated on the Bjerrum screen during this stage.

The objective signs of gradually developing impairment of venous circulation are engorgement of the venous tree or portions of it, and edema of the corresponding sectors of the optic papilla and/or of the retina along the involved veins. Careful comparison of both eyegrounds is imperative in these cases, as these phenomena are most often unilateral or when, as rarely, bilateral, they are only by great coincidence of equal degree. Especially if the venous occlusion develops in a patient with hypertensive disease, the presence of edema, unless carefully interpreted, may give rise to incorrect classification of the hypertension and in consequence tragically deprive the patient of the benefits of anticoagulant therapy.

Valuable subsidiary findings in the diagnosis of imminent venous occlusion are a unilateral absence of physiologic venous pulsation in the involved eye, or if physiologic venous pulsation is normally lacking, a great difference in the ease with which it can be produced in the two eyes by pressure upon the eyeballs.

Another finding of great diagnostic value, which is often present long before marked reduction of vision, is a dilatation or new formation of very tortuous and thin-walled vessels in one or more places at or near the optic disc. These point to an early attempt of collateral circulation, which may or may not be successful later on, depending upon preëxisting favorable or unfavorable anatomic conditions.

Anatomic vascular relations in fundi

In addition to early recognition of the subjective and objective danger signals of imminent retinal venous occlusion, a knowledge of peculiar or unfavorable anatomic vascular relations in a patient's fundi is of considerable value. Such conditions as multiple crossings of the same artery and vein or congenital loops and twists should be noted in all still-normal fundi of patients with essential hypertension, diabetes, and so forth, because the first evidence of venous circulatory disturbance may develop in these places.

Whenever the superior temporal vessels show such an anomaly, it should be reported to the internist with an explanation of its possible future importance in the development of a visual disturbance and the neces-

sity for prompt anticoagulant therapy in that case. Close observation of this area should be urged. This can be done by the internist, who is consulted more regularly by the patient, with an occasional ophthalmic consultation. Knowing about the possibility of a future treatment with anticoagulants upon short notice, the internist can collect certain data as blood typing and so forth, without losing precious time later on.

The patient himself should be told casually, without making him apprehensive of anything, to report any kind of visual disturbance without delay.

All these precautions and observations, if made routinely, take surprisingly little time but pay big dividends in preserving vision.

Role of venous stagnation

Among the factors favoring primary thrombus formation, stagnation deserves special emphasis. It occurs in senility with marasmus and low blood pressure, also in blood dyscrasias, and during certain phases of arterial hypertension. Loss of vision over night is a frequent and characteristic complaint in these cases.

In the hypertensive patient two different situations may lead to such marked slowing of the venous retinal circulation as to cause stagnation. Considerable reduction of a previously prolonged high systemic pressure is the more frequent of the two. Careful analysis of the history and general status of the patient often shows that the venous occlusion developed during a period of relatively low blood pressure usually much to the surprise of the general physician, who considered the patient much improved. The eyegrounds should be examined frequently and with special care during such periods of lowered systemic pressure, regardless of whether the reduction was spontaneous or was attained by therapeutic measures.

The second cause for venous stagnation in hypertensive patients is a sudden diminution of the retinal blood volume by widespread arterial spasm. The resulting slowing of the venous flow may reduce the pressure within the central vein to a point so much lower than the intraocular pressure that the vein collapses temporarily. A mild degree of preëxisting vascular sclerosis would facilitate thrombus formation at the place of lowest pressure within the central vein (Seidel[3]).

Prophylactic anticoagulant therapy at the first sign of venous congestion is sufficient in the first situation, and should be combined with antispasmodic therapy in the second condition.

Drugs favoring thrombus formation

Checking on the circumstances which may favor thrombus formation by various mechanisms, the effect of certain drugs should not be overlooked. Experimental evidence points to considerable clot-promoting properties of penicillin (Macht[4]), and this risk should be kept in mind in giving intensive penicillin therapy to a patient in whom the already described predisposing factors exist.

Digitalis is another example of a drug which is frequently administered to this type of patient, and one which may promote stagnation in the peripheral circulation by diminishing the venous return.

These side effects of such widely used drugs could be antagonized by simultaneous administration of dicumarol.

Case reports

The following report of five clinical cases will illustrate most of the statements made.

Case 1

History. K. J., a woman aged 62 years, complained of attacks of right visual obscurations of increasing frequency and duration during the past seven months. Left central vision was lost after a contusion 25 years ago.

The patient had had essential hypertension for the past 10 years and moderate generalized arteriosclerosis, but no physical symptoms other than failing vision of the right

eye. The blood pressure varied from 160/90 mm. Hg to 210/100 mm. Hg, and there was mild cardiac hypertrophy.

Two months prior to the first examination she had been hospitalized elsewhere and dicumarol had been given to her for two weeks, but was discontinued because no obvious subjective or objective improvement of her condition resulted. As a last resort

Fig. 1 (Klien). Venous retinal tree in the right eye in Case 1 before dicumarol therapy. Only the inferior temporal artery is sketched. Tremendous congestion of veins, edema of inferior half of optic disc, many delicate new vessels on disc, hemorrhages along inferior veins. Vision: 0.6—3, J3.

lumbodorsal sympathectomy was suggested.

Ocular findings. At the time of the first examination, in consultation with the neurosurgeon prior to the sympathectomy, the ocular findings were: Corrected vision, R.E., 0.6 + 1, J3 with difficulty; L.E., 1/200.

Right fundus (fig. 1): the lower half of the optic disc was edematous with a network of delicate newly formed vessels over its nasal border. There was tremendous engorgement of the venous tree, especially of the central vein, which was visible at the bottom of the cylindrical excavation up to the point where it entered the cribriform plate.

Retinal edema and numerous flame-shaped hemorrhages accompanied the entire course of the inferior temporal vein. There was no uniform attenuation of the arterial tree but considerable arteriolar- and arteriosclerosis.

In the left fundus, the arterial tree was similarly affected, but sclerosis of the larger branches was slightly less pronounced and the caliber of the veins was normal. There was an old macular hole.

Anticoagulant therapy for an extended period was advised, but sympathectomy was carried out. The patient was examined again six weeks afterward, when retinal edema and venous dilatation in the right fundus were more pronounced and the central vein appeared congested to the bursting point. Visual obscurations had continued and become more severe. Dicumarol therapy was urged again and started one month later on September 5, 1947.

Dicumarol therapy. After an initial three weeks' period of hospitalization, dicumarol has been continued ambulatory up to the present time. The first dose of dicumarol consisted of 400 mg. Administration of 100 mg. for the following three days reduced the prothrombin level to 49.1 percent. For the following four days 50 mg. daily were given, which resulted in a prothrombin level of 13 percent. After a pause of one day, 50 mg. were given again and continued every other day throughout the next three months, keeping the prothrombin level between 20 and 25 percent. After this time, during which the visual obscurations gradually disappeared, a prothrombin level of between 25 and 30 percent was considered sufficient, which was obtained by a dose of 50 mg. on two successive days interrupted by one day.

Results. On March 3, 1948, vision in the right eye had improved to 0.8 + 3 and J1 without difficulty.

The trunk of the central vein was again of normal caliber and a new large venous collateral entered the deeper layers just nasal to the optic disc. The general venous en-

gorgement, the retinal edema, and the hemorrhages had disappeared (fig. 2).

At the present time the patient has been free of symptoms for the past 10 months and has regained a right visual acuity of 1.0, and J1. A new venous anastomosis between a branch near the optic disc of the inferior temporal vein and a macular branch of the superior temporal vein has formed during the past year.

Prothrombin determinations are made once a week by the two-stage method (Warner-Brinkhaus-Smith[3]) exclusively. Twice the patient has taken a holiday in the south, once in Florida and once in Bermuda, lasting four weeks each, during which time a weekly blood specimen was sent to the laboratory by airmail and special delivery. The patient could be advised promptly by telephone or cable concerning necessary changes in the dicumarol dosage.

Comment. This case illustrates particularly well the importance of time in prophylactic anticoagulant treatment. Expectations of spectacular results within a short time would indicate lack of understanding of the influences at work in the repair of such conditions, but if ample time is allowed and great care and good judgment is used in the control of the prothrombin level, the end result may be quite rewarding, as the case just reported and the following case demonstrate.

Case 2

History. The course of events in this case, from 1941 to 1943, has been discussed in detail elsewhere (Klien[1]). Only the salient features of this period are repeated here before bringing the history up to date.

Mr. C. G., then 64 years of age, was first examined five weeks after the onset of intermittent blurring of vision in the left eye accompanied by a sensation of fullness in the head and slight vertigo. He suffered from mild arteriosclerotic hypertension (blood pressure, 140/90 mm. Hg to 160/100 mm. Hg) and there was mild retinal angiosclerosis in both eyes. The left retinal veins were enormously dilated, the upper half of the left disc was edematous, and numerous small hemorrhages accompanied the course of the veins. Heparin therapy was advised immediately, but could not be carried out for four months because of lack of funds. During this period the impairment of venous circulation increased slowly and the left vision was reduced from the initial 0.5 to 4/200.

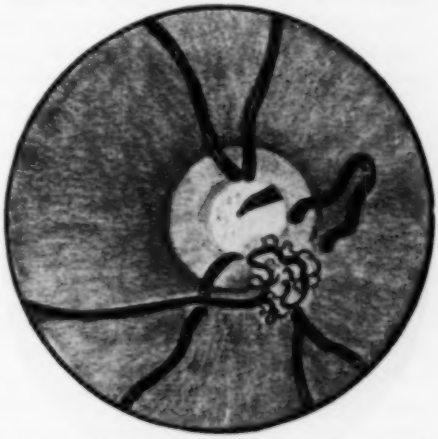

Fig. 2 (Klien). Same fundus as in Figure 1, 10 months after beginning of dicumarol therapy. The caliber of the retinal veins is normal; there is a large collateral branch on nasal half of disc, no edema, no hemorrhages. Vision: 1.0, J1.

Therapy. Three months after the first course of heparin treatment had finally been given the left vision had recovered to 1.2 and all evidence of the venous circulatory disturbance had disappeared.

Five months afterward, the second attack of marked left venous embarrassment was ushered in with headaches and long periods of visual obscurations. Heparin was given immediately, now combined with dicumarol, which under the name of dicoumarin was then still in the experimental stage. This patient is believed to be the first one on record to have received dicumarol for the treatment of retinal venous occlusion, and this therapy,

although not carried out in the well-established present day form, proved to be of more lasting benefit than heparin even then.

Only once, four years after the first dicumarol treatment, was there any recurrence of a left visual disturbance and venous circulatory embarrassment. Ambulatory dicumarol therapy was given at that time over a period of several months, and the patient, now 71 years of age, has been free of symptoms ever since with a visual acuity in the left eye of 1.5, and a general feeling of well being, not experienced for many years. Only a small fenestrated paracentral scotoma below the fixation area remained throughout the years.

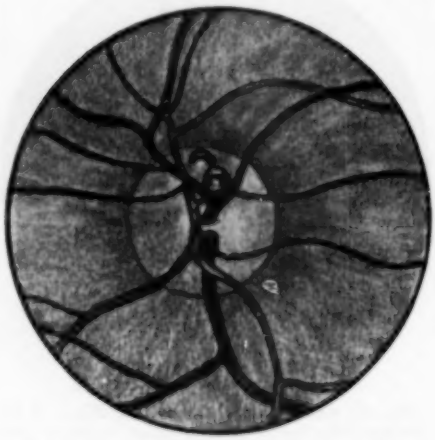

Fig. 3 (Klien). Fundus of the left eye in Case 2, eight years after occlusion of central retinal vein treated with heparin and dicumarol. Two venous loops are buried in the upper half of the optic disc. Twice during the eight years they became prominent and receded into the nervehead after dicumarol therapy. Vision: 1.2.

During the second attack, two venous loops were first noted projecting from the superior half of the left disc. They disappeared after the impairment of venous circulation subsided and reappeared again four years later during the period of premonitory symptoms of imminent venous occlusion of the third and last attack.

At present only the tips of both of these loops are visible (fig. 3), their main portion being buried again within the optic papilla.

Comment. In this patient apparently two objectives of anticoagulant therapy were obtained, time for the development of useful anastomotic channels, and reduction of stress upon the original venous wall to permit repair.

The new collaterals became clinically visible five months after the first course of anticoagulant treatment, that is, 10 months after the first observation of visual disturbances.

CASE 3

This case is discussed in retrospect, because the patient was under observation prior to the advent of anticoagulant therapy in its present form.

History. L. A., a woman, aged 57 years, entered the medical clinic at Northwestern University in November, 1939, for the treatment of essential hypertension. The blood pressure recordings at that time varied from 250 to 280 mm. Hg, systolic, and from 120 to 160 mm. Hg, diastolic. The electrocardiogram showed moderate left axis deviation. Left heart strain was stated on the medical record.

Under the usual management, blood pressure was gradually reduced, and in February, 1940, was recorded as varying from 158/90 to 166/92 mm. Hg. Several weeks afterward, it began to rise again and during the first weeks of August, 1940, was between 235/120 and 250/100 mm. Hg. Another low level was reached during the first two weeks in September, 1940, with 188/92 and 184/92 mm. Hg on several occasions. In September, 1940, it was again 255/115 mm. Hg. A note was made that during the entire period of observation the patient felt physically the best at a blood-pressure level averaging 215/115 mm. Hg.

The first eye examination was made in December, 1939. The patient's ocular complaints consisted of intermittent visual obscurations for the past year. Corrected vision

was: R.E., 0.5; L.E., 1.5. Photographs of the eye grounds were made three weeks later on January 16, 1940.

Further entries on the record of the eye clinic mentioned a sudden loss of vision in the right eye due to a massive vitreous hemorrhage on September 25, 1940. The last entry in October, 1940, recorded vision as: R.E., 8/200; L.E., normal.

It was the discovery, in 1947, of the old photographic records, which led to a re-evaluation of the history and findings of this case with recent advances of anticoagulant therapy in mind.

The fundus photograph showed the following findings: The margins of the right disc were ill-defined excepting a short stretch temporally where they were normal. The left disc was normal. There was no generalized attenuation of the arterial tree in either eye, but considerable arteriolar and arteriosclerosis, indicated by augmented, but uneven, brilliancy of the central light reflexes, marked arteriovenous compression, and irregularities of arterial caliber. There was good visibility of the smallest arterioles, and of the first bifurcation of the central artery in both eyes. Some of the venules in both macular areas had a typical corkscrew appearance.

The retinal veins in the right eye were more tortuous and slightly wider than those of the left eye, especially the ones in the lower half of the fundus, which were also accompanied by a slight retinal haze. There was no retinopathy in either eye.

The fundus picture of the right eye was interpreted at that time as Group V, that of the left eye as Group I of the Gifford classification.

Comment. The fundus findings in both eyes were typical of an essential hypertension of considerable duration in a well-advanced sclerotic phase. The only difference in the findings of the two eyes was the venous congestion in the right eye and the resulting edema of disc and retina, indicating an impairment of venous circulation, which led to a massive hemorrhage into retina and vitreous and loss of vision of this eye eight months later.

It seems more than probable in the light of our newest experiences with anticoagulant therapy, that the vision of this eye, with symptoms as early as eight months prior to the completed venous occlusion, could have been saved by prolonged anticoagulant treatment, promptly started at a time when the subjective symptoms were limited to intermittent visual obscurations and a somewhat reduced central visual acuity, and the objective findings to incipient venous congestion and collateral edema.

CASE 4

History. R. D., a woman, aged 52 years, complained of impairment of left vision for one week. She had had an essential hypertension for 22 years with a systolic pressure varying between 150 and 220 mm. Hg. Ten years ago she underwent a thyroidectomy.

Corrected vision was: R.E., 1.0 + 3 and J1; L.E., 0.3 − 1 and J6 with difficulty. There was a five-degree paracentral scotoma with the fixation point near its upper margin.

Fundi examination. The optic discs were normal. There was no generalized contraction of the arterial trees, but second to third degree of retinal angiosclerosis was present. The first macular branch of the left superior temporal vein was apparently occluded by a crossing, sclerotic artery and a voluminous retinal hemorrhage accompanied this vein from its delicate origin to this crossing. Some hemorrhagic imbibition of the retina extended downward into the foveolar region. The entire left venous tree appeared congested as compared to the right and the physiologic venous pulsation, which was distinct in the right fundus, was completely absent in the left.

From these findings it became obvious that a marked circulatory disturbance in the central vein was already present in addition to the macular branch occlusion, and dicumarol therapy was advised.

Dicumarol therapy. The patient received

dicumarol for six weeks. After an initial hospitalization of three weeks it was given ambulatory with a biweekly determination of the prothrombin level, which was kept between 30 to 35 percent. At the end of the sixth week the prothrombin dropped to 25 percent (the prothrombin determinations were carried out in a small suburban hospital) and there was a severe renal hemorrhage, which reduced the patient's erythrocyte count to 1.6 million. At the present time, two months after termination of the dicumarol treatment, her blood count is normal again.

It is planned to resume dicumarol administration, keeping the prothrombin level around 50 percent, because, in this case, its purpose is purely prophylactic. Inaccuracies in the prothrombin determination at this level are less dangerous and yet even a 50-percent reduction over a long period of time would seem beneficial as a preventive measure.

The patient's ocular findings at the present time are: Corrected vision, R.E., 1.2; L.E., 1.0 − 2 and J1. The macular hemorrhage has receded from the foveolar region. The congestion of the left venous retinal tree has disappeared and physiologic venous pulsation has returned, but is not as lively as that of the right eye.

CASE 5

History. C. G., a man, aged 66 years, had first noted six months ago that vision in his right eye was slightly poorer than the left. Three months ago the right vision began to fail rapidly and at that time he consulted his ophthalmologist, who recorded a right visual acuity of 0.6. During the past four weeks there was still more rapid deterioration of the right visual acuity, which was 0.1 at the time of the first examination. Uncorrected left vision was 1.0. There was a 10- to 15-degree right central scotoma with the fixation point near its lower border.

Fundus of the right eye. The optic disc was slightly edematous in its inferior half, there was marked retinal edema with numerous small and medium-sized retinal hemorrhages throughout the macular region, especially marked in the lower half. There was marked engorgement of the entire retinal venous tree with isolated hemorrhages scattered as far as the equatorial region, but the most acutely embarrassed branch was the inferior temporal vein, which was crossed twice by a sclerosed artery.

There was only a mild degree of angiosclerosis in the left fundus.

Dicumarol therapy. The patient was hospitalized for 10 days during which dicumarol therapy was started. It was continued ambulatory in another town, where also the prothrombin determinations were made. After four weeks of ambulatory treatment, at a prothrombin level of 19 percent, blood appeared in the urine and dicumarol was discontinued. At that time, vision in the right eye was 8/200. The macular edema and the number of hemorrhages appeared somewhat increased.

Soon afterward the patient left for a southern resort, where he was seen again, about four months after termination of the dicumarol treatment. Vision was: R.E., 0.2; L.E., 1.2. The retinal edema and the hemorrhages had disappeared. The large veins showed some irregularities of caliber. It is noteworthy that the vision of the left eye had also improved, from 1.0 to 1.2.

Comment. It is impossible to estimate the exact role of the short anticoagulant treatment in the unexpected improvement in this case.

This case is mentioned here because it illustrates the slow development of venous occlusion, and the ample opportunity for early preventive therapy which it would have afforded. The congestion, at least of the inferior temporal vein with its unfavorable anatomic relations, must surely have been present at the time of the patient's first visit to his ophthalmologist, when vision had been reduced to 0.6.

It also shows, just as the preceding case,

that the crux of ambulatory dicumarol therapy is the accuracy of the prothrombin determinations.

Discussion

The two-stage method (Warner et al.[5]) of determining the prothrombin level has proved to be more reliable than Quick's one-stage procedure. The main difficulty in obtaining completely uniform and trustworthy readings is the lack of standardized commercial reagents at the present time. Such reagents will be available on the market in the near future* and this will greatly increase the number of laboratories where reliable prothrombin determinations may be carried out.

The basic prerequisite for safe dicumarol therapy is access to such a laboratory, where the patient's requirements for the desired prothrombin level can be standardized and where biweekly or weekly prothrombin determinations can be carried out when the patient become ambulatory. Patients living within a considerable radius from a metropolitan center with these facilities may send their blood specimen by airmail and special delivery and receive necessary instructions within 24 to 36 hours.

Recent reports in the literature (Olwin,[6] Wright,[7] Foley and Wright[8]) confirm that, with such precautions, ambulatory dicumarol therapy does not hold any more hazards than treatment in the hospital.

Most of the reports relating serious complications after dicumarol administration were made in the early days of this therapy, or show lack of proper supervision of the changing prothrombin levels, or even complete omission of initial prothrombin determinations. Dicumarol administration without proper preparation of the patient for it should be considered criminal negligence, bringing, by its disastrous consequences, discredit upon a drug which has proved already to be extremely valuable in the hands of a careful and discriminating physician.

* Oral communication, J. H. Olwin.

Summary and Conclusions

1. A greater effort than heretofore should be made to render anticoagulant therapy in retinal venous occlusion preventive rather than curative by early recognition of predisposing factors and of the subjective and objective premonitory signs herein discussed. Irreparable structural damage to the retina by massive hemorrhage and, in the older patient, sluggishness of the physiologic mechanism for absorption of hemorrhage from retina or vitreous make the accomplished venous occlusion a rather destructive event with a poor outlook for functional recovery.

2. Preventive anticoagulant therapy has two main objectives—to gain time for the development of patent collateral channels, and to permit repair of damaged venous endothelium by reducing strain upon the vessel wall.

The value of aiding the natural resources in imminent venous occlusion by gaining time for the establishment of patent collaterals has not been properly recognized. Reconstructions of the central vessels in eyes lost from venous occlusion (Klien[3]) show in almost every instance one or more large, new or preformed branches, which might have taken over for the central vein in due time. The clinical picture (Klien[3]) of cases with spontaneous anatomic, if not visual, recovery show often 2 and 3 apparently functioning new channels. They seem to be the rule rather than an exception and it is hoped that, in the future, they will play a widely recognized role in the preventive therapy of venous occlusion. For the dual purpose of this treatment, it has to be carried out over a long period of time, even years.

3. For the prolonged anticoagulant effect, ambulatory dicumarol administration as outlined above in the report of Case 1 and in the pertinent literature elsewhere (Olwin,[6] J. Macy, Jr. Foundation[9]) has proved to be satisfactory. The cumbersome necessity for frequent prothrombin determinations is

counterbalanced by the inexpensive and easy oral administration of the drug. The time required for effective dicumarol treatment differs in different patients, depending upon the severity of the initial symptoms.

A careful ophthalmoscopic examination three weeks after its arbitrary discontinuation, and repeated once or twice afterward in intervals of several weeks, will uncover recurrent signs of venous circulatory disturbance and indicate the necessity for extension of the therapy. The time necessary for formation of adequate collateral channels must vary with preëxisting anatomic conditions. In the cases observed by me an average of six months elapsed before clinical evidence of their existence appeared.

4. In preventive administration of dicumarol, the length of time over which it is used is of greater importance than a radical reduction of the prothrombin level to 20 or 25 percent such as is necessary for curative purposes. The preventive management may be started with curative doses during the patient's initial period of hospitalization combined with heparin in selected cases to utilize the latter's inhibitory influence upon fibroblastic growth, and afterward be continued ambulatory with a prothrombin level of 50 percent for many months or years. This measure would increase the safety of the procedure until such time when improved commercial reagents will be on the market, which will make control of dicumarol therapy more accurate through more reliable prothrombin determinations by the two-stage method.

5. Both internist and general practitioner should be taught that prevention of retinal venous occlusion is possible, that it should be the main aim of anticoagulant therapy in these cases, but that an exacting teamwork with the ophthalmologist is essential for it, at least at the present time. It is possible that in the future, preventive anticoagulant therapy will be more widely used in hypertensive and cardiovascular diseases, which would automatically reduce also the incidence of retinal venous occlusion. Another future development may be the combination of therapeutic agents, which have a side effect of creating conditions favoring thrombus formation, as digitalis and possibly penicillin, with anticoagulants.

7427 South Shore Drive (49).

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GONIOSCOPIC OBSERVATIONS DURING THE EVOLUTION OF AN ACUTE IRIDOCYCLITIS

J. François, M.D.
Ghent, Belgium

In a report on gonioscopy, read to the Société Belge d'Ophtalmologie in February, 1948, I described the gonioscopic manifestations of iridocyclitis. These manifestations are, firstly and early, congestion of the root of the iris with edema and exudates, which are deposited on and in the different parts of the corneal angle; secondly, but later, the pigmentation of the angle and the goniosynechias.

The inflammatory edema of the ciliary border of the iris and the rare goniosynechias, which are due to the approximation of the two walls of the angle by swelling of the iridic wall, may be localized at any part of the angle, at the top, bottom, or laterally.

On the other hand, the pigmentation, the exudates, and the goniosynechias, which are almost always due to the exudates, are present, so to say, exclusively at the level of the lower part of the angle. The goniosynechias may, or may not, exist in the absence of posterior synechias. They can be forming at different times—before, during, or after the posterior synechias.

Instead of giving drawings, illustrating these facts by reproducing a demonstrative aspect of the most typical cases, I would like to show by a series of figures the gonioscopic evolution of the same lesion during the same affection. This will help us better to understand the formation and the connection, the genesis and the development of several stages observed at the level of the angle of the anterior chamber.

As Amsler said, we must not adhere to appearances of the present moment but keep an account of time and duration. A fixed and static morphology, which has been shown to be clearly insufficient, must be abandoned to refer to dynamic iconography, according to the expression of Onfray.

Case report

History. On April 5th, a woman, aged 40 years, came for examination of her right eye, which had been painful and red for three days. There was an acute iridocyclitis which was characterized by a few keratic precipitates, leukocytes in the aqueous, and a large posterior synechia of the iris at the 5:30-o'clock position.

At the age of 25 years, she had had typhoid fever, and, at the age of 37 years, a frontal right sinusitis. A left ovarectomy had been done when she was aged 32 years. The patient had a daughter, aged 12 years, in good health. She had had one miscarriage. She has never suffered from rheumatism. She was completely toothless.

The general physical examination was negative. Simply to be noted was hard breathing, a positive appendicular point, an intolerance to fatty foods, and a syndrome of hyperfolliculinism.

The blood-pressure was 14/8 by Vaquez. Neither sugar nor albumen was present in the urine. The B.G.S., the Hecht, and the Kahn reactions were negative. The gono-reaction was positive. The speed of sedimentation was 45 minutes. The hematology analysis gave: Hemoglobin, 97 percent; red cells, 4,520,000; leukocytes, 6,900; neutrophiles, 53; eosinophiles, 9; basophiles, 0; lymphocytes, 32, monocytes, 4. The radiography of the lungs showed no abnormality. In conclusion, from an etiologic point of view, chronic gonorrhea was to be suspected.

Treatment. In addition to the instillations of atropine and hot compresses, I prescribed strong doses of adiazin and injections of milk.

Course. On April 7th, the keratic precipitates were larger and more numerous; the posterior synechia of the iris had spread

farther and occupied the pupillary section included between the 4- to the 5:30-o'clock positions.

GONIOSCOPIC EXAMINATION

By this time the gonioscopic examination showed (fig. 1) that the angle of the anterior chamber had a medium width. The ciliary-body band showed a dark gray color. Here and there iris processes spread out from the root of the iris and flowed through the ciliary-body band, but did not go beyond the scleral spur which was not clearly visible. The trabeculum, of rather a pale gray color, showed precise limits, although the line of Schwalbe was not very clear; the inferior part showed a few pigment dots, which were more numerous in front than behind. Up to this point there was, in reality, nothing abnormal.

Below, however, toward the 6:30 o'clock position, at the level of the trabeculum, was observed a small, rather thick mass, the size of a pinhead, which was composed of a whitish exudate. It was prominent in the anterior chamber, invaded the ciliary-body band, and expanded to the root of the iris. This exudate contained some grains of pigment of a dirty brownish color. Farther inside, towards the 5:30-o'clock position, there existed, at the level of the ciliary-body band near the visible edge of the iris, three small protruding spots, very limited, also formed by white exudate. At the top and laterally, the angle did not show the least abnormality.

During the following days, although the keratic precipitates increased but little and no new posterior synechias were formed, the exudates increased and continued to accumulate in the inferior part of the angle, which, in the end, was completely invaded (fig. 2 sketched April 14th). From the 4:30- to the 7:30-positions, the angle was blocked by an abundant exudate, very thick and opaque, yellowish in front and pinker at the back. This exudate almost completely overlapped the root of the iris and the line of Schwalbe; it had a dirty aspect, owing to the presence of fine pigment dots. None of the different features of the angle were recognizable, neither the ciliary body band nor even the trabeculum, although the pigment was transparent, having a soiled hazy tint. At the top and laterally, there was not the least trace of exudate. It should be noted that the tension of the eye was not raised.

By April 16th, the exudates began to be resorbed. The angle became progressively clearer and the keratic precipitates also disappeared. On April 28th, there was no exudate except in the most declivous part of the angle, that is, at the 6-o'clock position, where it was in fact the most abundant (fig. 3). At the level of the ciliary-body band, there was a yellowish, dirty white mass of unprecise limits, which slightly overlapped the root of the iris as well as the scleral spur. More laterally, the ciliary-body band, with its iris processes, reappeared intact and normal. The trabeculum was once more visible, but the pigmentation had been modified—it was distinctly more pronounced than before and was especially abundant at the 6-o'clock position where the pigmentary grains assembled again to form spots more or less separated.

During the following days, the cure progressed until, about the middle of May it was complete. The posterior synechia of the iris disappeared and the pupil recovered its regular round shape. The keratic precipitates had disappeared and the eye was white once more.

On June 11th, the final gonioscopic examination gave evidence of a few sequelae (fig. 4). At the 5-o'clock position, there was a tentlike ciliary goniosynechia and, at the 6-o'clock position, a rather large trapezoidal trabecular goniosynechia, which was attached to a slightly undulated edge a little in front of the scleral spur. On each side of this goniosynechia was seen, at the level of the ciliary-body band, tiny pigmentary grains.

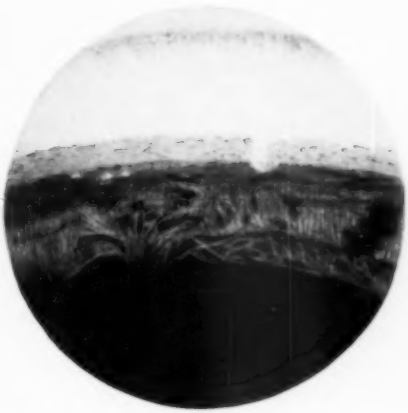

FIGURE 1

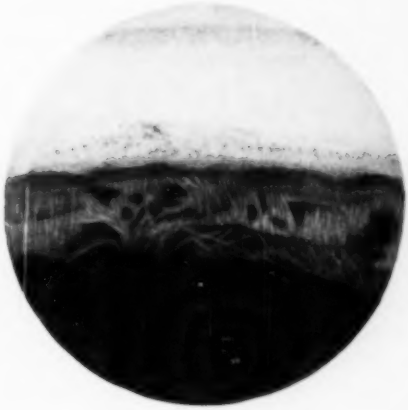

FIGURE 2

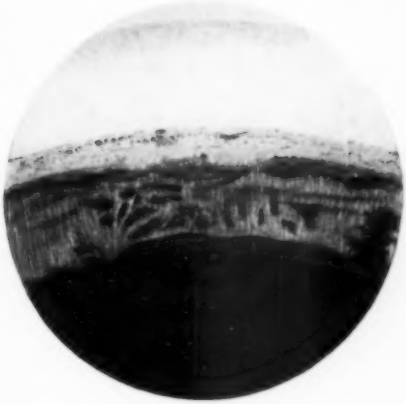

FIGURE 3

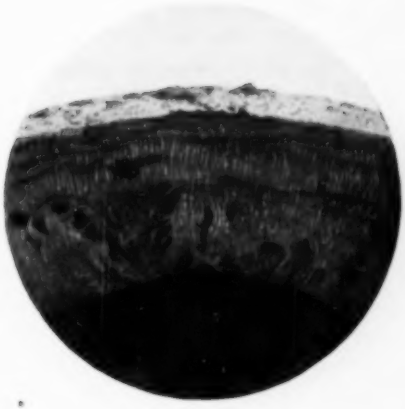

FIGURE 4

FIGS. 1 TO 4 (FRANÇOIS). GONIOSCOPIC OBSERVATIONS DURING THE EVOLUTION OF AN ACUTE IRIDOCYCLITIS. (FIG. 1) SKETCHED ON APRIL 7TH. (FIG. 2) SKETCHED ON APRIL 14TH. (FIG. 3) SKETCHED ON APRIL 28TH. (FIG. 4) THE FINAL SKETCH MADE ON JUNE 11TH.

These grains of pigment could also be seen on the root of the iris. At the level of the trabeculum, the pigmentation had still been growing; the dark-brown pigment dots were especially abundant towards the 6-o'clock position and in the vicinity of the line of Schwalbe, where they agglomerate so as to form irregular spots, some of which overlapped the anterior limit of the trabeculum.

Discussion

During the evolution of an acute iridocyclitis, the successive gonioscopic observations showed:

1. The appearance of circumscribed exudates.

2. Increased quantity and spread of these exudates which, in the end, invaded and obstructed all of the inferior part of the angle.

3. Progressive resorption of the exudates and the simultaneous appearance of an abnormal pigmentation, which involved not only the scleral trabeculum but, to an equal extent, the ciliary-body band and the root of the iris.

4. The formation of a large goniosynechia.

It is to be noted that all of these inflammatory manifestations were confined to the level of the most declivous part of the angle of the anterior chamber. This suggests that the exudates, as well as the grains of pigment, are not, or at least not exclusively, formed on the spot but that they are drawn toward the inferior part of the angle where they are deposited by sedimentation.

The appearance of a peripheral synechia at the time of the resorption of the exudate clearly indicates the usual mode of formation of inflammatory goniosynechias which ordinarily result from the organization of the exudate. This explains their tardy production, often much more tardy than that of posterior synechias.

Summary

Figures 1 to 4, showing the gonioscopic evolution of the same lesion during the same case of iridocyclitis, give a better understanding of the formation and development of the exudates, pigmentation, and goniosynechias observed at the level of the angle of the anterior chamber. These inflammatory manifestations are almost exclusively located in the most declivous part of the angle, where both exudates and pigment are deposited by sedimentation and where the goniosynechias are formed by organization of the exudates and not by swelling of the root of the iris.

Avenue Pasteur 2.

Ophthalmic Miniature

No modern remedy has been received by the profession with such general enthusiasm, none has become so rapidly popular, and scarcely any one has shown so extensive a field of useful application as cocaine, the local anesthetic recently introduced by Dr. C. Koller, of Vienna.

Herman Knapp, "On Cocaine and its Use in Ophthalmic Surgery." *Archives of Ophthalmology*, **13**:402 (December) 1884.

THE PRESENT STATUS IN THE TREATMENT AND PREVENTION OF TRACHOMA*

MAX HIRSCHFELDER, M.D.
Centralia, Illinois

During the last 15 to 20 years the fight against trachoma all over the world, and especially in the United States, has been much more intensive and better organized than during the 19th century and in the early decades of this century. During the last 10 years, this fight has been tremendously aided by the discovery that certain chemical and biologic agents have a beneficial and rapid influence on trachomatous disease and that these new drugs simplify the problem of treatment.

There is little doubt that the incidence of trachoma in the United States has become less. Even in the eye hospitals of our large cities, which often were full of referred trachoma patients from the endemic regions in the Ozarks, the incidence of new trachoma has dropped considerably. It would be a most difficult task nowadays to obtain, for instance in Southern Illinois which, 30 to 40 years ago, had widespread endemic trachoma, a fresh case of trachoma for demonstration at any certain time, because only very rarely does one see nowadays the granular follicles in the upper palpebral conjunctiva, the fresh and recent invasion of the cornea by superficial blood vessels from the upper limbus, the new superficial infiltration and the first epithelial corneal breakdown with this active pannus, and the pitiful picture of a patient blinking through tearing eyes, bent toward the ground to avoid the light.

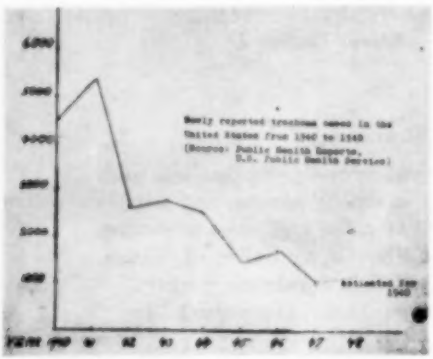

Fig. 1 (Hirschfelder). Newly reported trachoma cases in the United States from 1940 to 1948.

What one sees more frequently in daily practice are the patients who went through the fresh stages of the disease some 25 or 40 years ago. They exhibit the well-known scars in the palpebral conjunctiva, scars in all types and forms on the cornea, and the thin, shadowy vessels of inactive pannus. These patients quite frequently do not come to the office for their trachoma, which gives them no trouble, unless it is the old visual defect. They are mostly seen during a routine examination for glasses or other trouble not necessarily connected with trachoma. Occasionally, they return for treatment of a flare-up or a renewed breakdown of the corneal epithelium or for the repair of an ectropium and similar complaints. Sometimes they are seen as applicants for blind pension, because over seven percent of trachoma sufferers used to become industrially blind (Gradle).

It is quite evident that the picture of the morbidity, the stage, and the spread of trachoma has changed in this country. A graph prepared from the figures of the United States Public Health Service will illustrate a drop for the past eight years (fig. 1). The incidence of trachoma morbidity declined from around 5,000 per year for the whole United States to about 1,200.

Naturally, there is a fallacy in such statistics because they depend on the actual reporting of cases by physicians and other

* Read before the Chicago Ophthalmological Society, February 21, 1949.

medical personnel. If no report is made—and this was the case 20 years ago, and may still be the case in regions without adequate trachoma control—the figure will be low in spite of a high incidence. However, the statistics of the past 10 years should be more reliable, because the personnel of the various trachoma projects in the states where the disease is most prevalent is usually very statistically minded. They go out and look for new cases and if they find one, they report it.

This organized fight on a large scale is relatively recent in origin and not more than 25 years old. Several papers have appeared describing the fight against trachoma in our nation. Gradle[1, 2] spoke on several occasions of the situation in Illinois; Cosgrove[3] described the situation in Arkansas; Siniscal has reported on Missouri,[3a] representatives of the Indian Service[4] have repeatedly described the situation there.

Factors effecting trachoma decline

It would seem, therefore, to be a useful task to consider the various factors which have led to an apparent improvement in the trachoma incidence in this country, to coordinate the various experiences, and to analyze our present-day situation.

Higher living standards

We first have to consider certain changes which have been brought to the individual person and to the individual family, not as a result of treatment or of state efforts, but in consequence of a better mode of living. These changes greatly aided the organized efforts, some of which would probably have been doomed to failure without them.

While trachoma can affect anybody, rich and poor alike, it is well known that it is particularly a disease of the lower-income groups, of people who live in crowded rooms, of mountaineers in the backwoods, of people who come in Model-T Fords, rather than in Cadillacs.

Trachoma, originally brought to this country by the Spanish colonization and later by Slavic immigrants, spreads from one family member to the other through the use of one common wash basin and one common and, usually dirty, towel. The afflicted person was far from medical aid, separated from it by often impassable dirt roads and by long distances. The patient was unfamiliar with the most simple hygienic measures and not prepared for long and expensive treatment.

Today we have a road system in the United States which allows inhabitants of the more remote parts of rural districts to come to the treatment centers by car or bus without great effort. The importance of this fact is brought out by Apin[5] who reports on conditions in Latvia. Of the trachoma patients living close to treatment centers 75.9 percent were cured, while only 24.9 percent of those living in remote areas had such a beneficial result. The author states that wide separation of communities, even in as small a country as Latvia, is a deterrent to the fight against trachoma. The relative ease of transportation in the United States as compared with these European countries and, still more, with North Africa or China, plays a significant part in trachoma control.

It is unlikely that the common wash basin has disappeared entirely, but we can safely assume that the advent of indoor plumbing and personal cleanliness is spreading to remote areas. A recent confirmation as to the value of individual hygiene may be a report by Bodian[6] about trachoma in the Fiji Islands. Of 100 natives working at an army base, 22 percent had active trachoma, many cases being confirmed by the finding of inclusion bodies. However, not one of the 50 American soldiers stationed there from 1 to 3 years contracted the disease.

Effect of new therapeutic measures

The second important factor to consider in the decline of the incidence of trachoma is the effect of the new therapeutic measures. The time-honored use of the copper-sulfate

stick, of other caustics like alum or silver nitrate, the massage of the everted lids with or without chaulmoogra oil or, more recently with quinine bisulfide, the expression of follicles by grattage, the extensive use of mercurial antiseptics in washes or ointments—all this is well known to the ophthalmologist and does not have to be elaborated upon. Although all of these measures are effective in a large percentage of cases, they have to be employed regularly over a comparatively long period of time. They have not, however, lost their place in our medical armentarium.

To these older methods of treatment have now been added the newer and much faster chemotherapeutic agents, especially the sulfonamides. This group of chemotherapeutic agents has been employed since 1937 (Lian,[7] Loe[8]).

Most authors (Thygeson,[9] Guyton,[10], Hirschfelder[11]) recommend the oral usage of sulfanilamide, one-third grain per pound body weight a day during the first week, one-fourth grain during the second week and, if still indicated, somewhat less during the third week. Local application of neoprontosil (Cheney[12]), sulfanilamide powder, and as a solution of sulfacetamide (Lugossy[13]) has been suggested. Local usage of neoprontosil in trachoma has been disappointing in our experience. Sulfacetamide in 30-percent solution seems to be more effective.

Intravenous administration has not been used to any extent in this country, but the Russian literature mentions the preparation of "sulfidine," which is injected into the vein, 10 cc. of a 1.5-percent solution twice a day for adults, 5 cc. of the same concentration for children (Melik-Musian[14]). This kind of medication is said to "melt away" pannus crassus. Subconjunctival injection of sulfidine was found to be too irritating. There are by now innumerable reports describing the beneficial effects of such sulfa preparations as albucid, lutazole, and streptocide (Johannsen,[15] Ferrer[16]).

The intramuscular use of sulfanilamide in oil every four days or of sulfapyridine in oil in 10-percent suspension as a depot every 7 to 10 days is recommended by Lee and Rottenstein.[17] Thygeson[18] has lately substituted the oral medication of sulfadiazine for that of sulfanilamide and finds no difference in effectiveness.

Evaluation of the Sulfonamides

In evaluating the experiences of all these authors we find three distinct opinions. One group, an exponent of which is Thygeson, emphatically believes that the sulfa drugs are indicated in all fresh cases of trachoma, that they attack the trachoma virus and, by so doing, cure the disease. This group points out that inclusion bodies are rapidly disappearing on the third day of treatment and that correct dosage will clear up fresh uncomplicated trachoma in three weeks. Harley[19] expresses a similar opinion. Thygeson feels that failures of cure are due to inadequate dosage and time of treatment.

There is a second group of authors who are not convinced of the omnipotence of the sulfa drugs in trachoma. Julianelle and Smith,[20, 21] showed that conjunctival scrapings from trachoma patients remained infectious after exposure to sulfanilamide in vitro. They concluded that sulfa acts only as a bacteriostatic and not as a bacteriocidal agent.

Poleff[22] supports this view, but ventures the thought that the impaired virus might subsequently be completely destroyed by phagocytosis. Authors in this group stress the fact that follicular hypertrophy often tends to persist and that the older method of massage and expression are still needed in combination with chemotherapy.

Sory[23] goes so far as to say that sulfanilamide by itself only exceptionally arrests trachoma, that it is by itself less reliable than other known forms of treatment, and that its value is only in conjunction with other local forms of treatment which have been known for years. The same author also points to recurrences as proof that the dis-

ease is not cured by the drug. It is repeatedly pointed out that the corneal complication and pannus respond much more readily than the palpebral pathologic processes. Further, that the subjective relief is out of proportion to the objective findings.

Meissner,[24] describing Germans repatriated from Bessarabia to Munich, thought that only the superimposed conjunctivitis and the pannus were influenced but that not a single case was cured.

Finally, there is a small minority (Bhalero[25]) who deny any value in chemotherapy and prefer to stick to the older methods.

From my own experiences, I am inclined to side with Thygeson and his group. I have seen a few very active, succulent trachoma cases which had had no treatment of any kind and which were cleared completely in a few weeks by chemotherapy alone.

Naturally we ask ourselves; "Why is there this difference of opinion?"

I believe that the relative scarcity of fresh, recent cases of trachoma is one of the reasons. The older the case, the less satisfactory is the use of the chemotherapy. Another reason is a certain vagueness in the diagnosis, "Trachoma," especially in the trachoma territory.

There are a lot of children in southern Illinois whose fornices are bulging with follicles. Expression material never shows inclusion bodies. These cases never develop pannus, never suffer any ill effects or complications, and never respond to chemotherapy. There is no justification in calling, as has been done, such cases of folliculosis subclinical trachoma and then blame sulfa for failure to cure something which is not trachoma.

There are also many cases of follicular catarrh which show a mild inflammatory process (folliculosis may not show any inflammation at all) and which look suspiciously like beginning trachoma. In trachoma territory they can easily be taken for trachoma, and one must insist on the presence of beginning corneal pannus for a definite diagnosis of trachoma. These pseudotrachoma cases do not respond to sulfa drugs.

Sory's statement that in seemingly arrested cases there may be another flare-up is correct. A patient has to be observed at regular intervals, even though he seems cured. There is no doubt, however, that any 2nd or 3rd or 4th flare-up can be quickly controlled and seemingly cured by another round of the drug.

As has been stated, older cases may prove to be sulfa resistant. The patients come to the office with flare-ups and corneal breakdowns, which, however, in a great many instances are not due to a revival of the trachoma virus.

Sometimes these flare-ups are the result of trichiasis. Often they are due to a lowered resistance of the conjunctival and corneal cells, to an altered and impaired blood supply and tissue metabolism, to a poor ability to regenerate cells and, sometimes, to general poor physical health. These are breakdowns which develop in tissue impaired by trachoma many years ago. They develop in the run-down eyes of run-down people, just as marginal ulcers so frequently develop in elderly people.

Treatment, aside from the usual local therapy and corrective lid surgery, should include measures to build up the constitution rather than specific chemotherapy. Landau and Stern[26] have recently called attention to the discrepancies between the relatively mild palpebral and the severe corneal findings. Their theory of a vitamin deficiency as evidenced by ariboflavinosis points in the direction just mentioned.

Penicillin and other therapeutic agents

Penicillin therapy in trachoma has not been as intensively investigated as that of the sulfa group. There may be two reasons for this. First, sulfa is so satisfactory that there has been no need for extensive investigation. Second, penicillin is not as effective an agent. It is uncertain whether penicillin at-

tacks a virus disease like trachoma and many of the reported improvements may be due to subsidence of secondary infections.

Darius[27] reported the cure of 12 patients in 19 days of hospital treatment with penicillin (500 units per cc.) instilled into the conjunctival sac every one-half hour. These patients were still well six months later.

Sorsby[28] cites four cases from the literature in which the trachoma subsided under penicillin treatment and adds a few favorable cases of his own in which the conjunctiva was painted with a 2,500-unit per cc. penicillin solution for 12 days. These authors are not as enthused over penicillin, however, as others are over the sulfonamides. One should remember penicillin for sulfa-sensitive patients, nevertheless.

The Italian authors, Bietti and Pasca[29] investigated streptomycin. They conclude that it has no advantage over penicillin in trachoma cases. It is stated that improvement was slight and late.

Antimony potassium tartrate or tartar emetic given intravenously seems to have an influence similar to that of the sulfonamide group. Julianelle and his co-workers[30, 31] found an improvement in the advanced corneal findings of trachoma. They report only little change in the palpebral pathologic processes. The visual acuity of their patients improved and the toxic reactions were negligible. The trachoma virus seemed to be inactivated in vitro by this drug.

We finally have to mention experiments with tissue therapy by Russian investigators and the experimental use of snake and bee venom by German authors. None of these efforts have so far been followed up in this country nor have they led to any wide use in the described therapy.

Role of Public-Health Agencies

We have seen that improved standards of living as well as improved methods of treatment have had a beneficial influence on the number and severity of trachoma cases. A third and most important factor should now be added—the greater interest and better organized methods of public health agencies in combating the disease during the past 20 years.

Any public health campaign must have financial support and sufficient funds made available by sympathetic and far-sighted political bodies are a basic necessity. Compared to the eventual expenditure for blind assistance during subsequent decades these funds for prevention are relatively small. It is up to the medical profession to see that these funds are spent most wisely and most effectively.

It would, for instance, not be sufficient merely to pay the bills for people, who seek medical care for trachoma, or to make sporadic field surveys every few months or years. Such simple attempts to combat the disease would be sufficient if everyone who has trachoma were an enlightened patient and would be 100-percent coöperative. Unfortunately, such ideal circumstances rarely happen in the field of public health and especially not in the field of trachoma. I doubt that they happen even in the nations where a law forces the trachoma patient to be treated.

In order to combat endemic trachoma successfully, the following considerations are imperative:

There has to be an organized, continuous, and systematic effort by health workers to find the afflicted persons, to educate them in the prevention of spreading their disease, and to bring them to treatment regularly. While the disease is in an active stage, facilities should be made continuously available, where this treatment can be given in the best possible way. It is necessary to provide for the constant and regular follow-up of the arrested cases until the patients eventually die, which may be years later. Physicians, nurses, field workers, and social agencies have to work as a team to check on treated cases, to catch flare-ups and re-infections, to examine possible contacts and, finally, to keep a controlled district under control.

Hospital system of control

There are two ways to achieve this objective: One is by means of a well-equipped trachoma hospital. From this centrally located hospital, teams go out regularly into distant regions for field surveys. Active and fresh cases are referred to the hospital as in-patients for work-up and necessary medical or surgical treatment. Missouri, Kentucky, and Tennessee operate under this plan, the hospitals being located in Rolla, Missouri, and Richmond, Kentucky.

This plan has the advantage that the acute case is kept under strict survey and is assured of regular maximum treatment. However, as Figure 2 seems to indicate, this plan has failed to bring the disease under complete control and to eradicate it.

Missouri reports as many or more yearly cases as before. The incidence in Kentucky has declined after 22 years of operating the Richmond Trachoma Hospital, and after

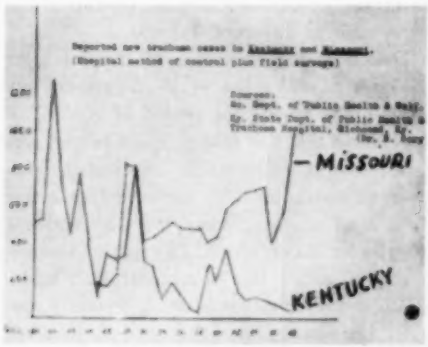

Fig. 2 (Hirschfelder). Reported new trachoma cases in Kentucky and Missouri where the hospital plus field surveys method of control is used.

33 years of some kind of control. Dr. Sory, however, stated in a letter, that he believes that this decline is not a real one, but that the figure is small due to lack of adequate field surveys and lack of a field nurse.

The situation in Tennessee compares to that in Kentucky, with the Richmond Hospital receiving the severe cases and local oculists treating the mild cases. Only extensive field surveys can give assurance that the improvement (fig. 3) is a true one based on a real decline in trachoma incidence.

Without wanting to detract from the excellent and highly beneficial work carried out in these institutions, I want to list the following disadvantages of the hospital system:

1. The bed capacity is limited. In the first

Reported Trachoma Cases, State of Tennessee.
Control measures started in 1929.
Field surveys, diagnostic clinics, treatment of indigents in clinics and hospitals.
Source: Dept. of Public Health State of Tennessee.

Fig. 3 (Hirschfelder). Reported trachoma cases in Tennessee which uses field surveys, diagnostic clinics, and treatment of indigents in clinics and hospitals.

years of newly established control measures it may be too limited to take care of all the patients needing treatment.

2. Field surveys are usually not continuous and a fresh epidemic in a certain region may spread for several months before it is detected.

3. A majority of trachoma patients are not totally disabled. While they unquestionably are in need of treatment, they do not necessarily need hospitalization.

Field clinics or dispensaries

The other way in the attempt to control trachoma, employed here in Illinois and, to a similar extent, in Arkansas, is built on a system of permanent field clinics or dispensaries. The Illinois System was developed by Gradle in close collaboration with the Illinois Society for the Prevention of Blindness[22] and the Department of Public Wel-

fare. It was started in 1934 and has been carried on ever since.

Five clinics were established in southern Illinois about 30 to 40 miles apart. Each is manned by a trachoma nurse responsible for her district. A staff of field workers is attached to each clinic with the task to find the cases, to encourage regular visits to the

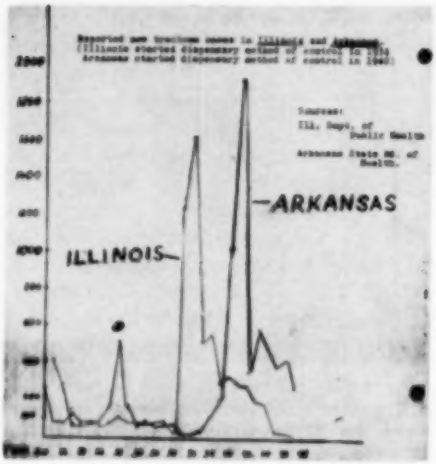

Fig. 4 (Hirschfelder). Reported new trachoma cases in Illinois and Arkansas which use the dispensary method of control.

clinic, and to check on each case, even after it has been pronounced arrested.

Each clinic operates and gives treatments three times a week and, on one of those days, the oculist who serves all five clinics makes the necessary diagnosis, instructs as to treatment, and carries out the necessary surgical measures. All entropion or ectropion surgery, removal of tear sacs or pterygiums, can well be done on ambulant patients, and I never heard of an accident.

Regular free bus service converges from all points of the district toward each of these clinics on treatment days. This bus service is unique in Illinois and constitutes an important factor in the success of the control.

Figure 4 shows how a very large number of trachoma cases were diagnosed during the first few years of the established control, both in Illinois[33] and Arkansas.[34] Figure 4 then shows, in contrast to Missouri and Kentucky, a continuous decline in response to continuous and unabated vigilance. We are now at a point where, 15 years after the start of operations, the number of new cases found in Illinois is near the vanishing point. This decline is not an apparent one (due to the lack of field nurses) but it is a true reflection of the negligible number of new trachoma cases.

West Virginia operated a movable field clinic in a truck-trailer for two years, but discontinued this because of lack of funds. This state now has two field clinics in the two most involved counties. A trailer system is probably successful, if the area is relatively small and the patients can be treated frequently enough. In a large area, regular visits to the same district are not frequent enough. Continuity of treatment and, with it, control are bound to suffer, unless a sufficient number of movable units operate at the same time in different districts.

Discontinuing measures of control after the lapse of only a few years jeopardizes any gains made during the period of control. It may mean that the money spent helped certain individual patients. It constituted, however, at least a partially useless effort as far as control of the disease from an endemic standpoint is concerned. The cost of keeping a region, which has been controlled, under continued observation is small, certainly considerably smaller than the expense involved during eradication of the active stages of trachoma.

No state-wide measures have recently been undertaken in Oklahoma, which at present relies on local county measures.

Work of the Indian Service

Finally, one has to mention the splendid work carried on by the United States Indian Service. Thygeson, Forster, McGiboney, and Richards have repeatedly published statistics

showing the successful fight carried on on the Indian reservations. According to McGiboney's report, the trachoma incidence among Indians dropped from 20 percent to 7 percent between 1939 and 1943 following the introduction of sulfanilamide treatment.

Comment

If one summarizes all these experiences, it seems that the dispensary method with its multiple stationary field clinics eradicates trachoma in a given region faster than a trachoma hospital. It is possible that, in a country with acute endemic trachoma, the addition of a centrally located trachoma hospital is desirable in order to refer the worst cases for isolation and for continued observation and treatment. It seems, however, that a single hospital, even if it sends regular diagnostic parties into the different districts, cannot by itelf solve the problems of an endemic disease in as short a time as multiple dispensaries.

In an article published by Gradle in 1935 the number of white persons afflicted with trachoma was estimated at 33,000. It seems likely that the incidence of fresh, active trachoma has since decreased and that most cases now found are in the late stages.

The United States is not alone in this fight. Russia[35,36] reports a reduction of the incidence of trachoma between 66 percent and 75 percent in certain districts. This was achieved mostly by the dispensary method of treatment. An improvement in the situation in Egypt is reported by Massoud[37] who envisions trachoma-free schools. He reports that 70 percent to 80 percent of the school children are trachoma free.

The committee on trachoma of the Pan-American Congress of Ophthalmology estimates that there are one million trachoma cases in North and South America. Most of the American nations are now undertaking measures against the disease. The Illinois system merits their attention and possible imitation. There was not a single Stage-1 case in Illinois during 1948. When a trained personnel is on the lookout for it, one can assume that this is a correct report. Continued control is needed to assure the final and complete eradication which Gradle envisioned in the early 1930s and which now seems to be within the realm of possibility.

Summary

Statistical evidence shows a decline of trachoma in the United States. Easier access to treatment facilities, better hygiene, the introduction of chemotherapy, and well-organized public effort to control the disease are the reasons for this decline.

A comparison of the statistics of various states would seem to indicate that multiple field dispensaries in various districts bring trachoma under more certain control in a shorter time than a single trachoma hospital. A hospital may have to be opened in an area in which there is severe and wide-spread endemic trachoma.

408 West Second Street.

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KERATOCONJUNCTIVITIS SICCA*

A REVIEW WITH A SURVEY OF 121 ADDITIONAL CASES

JOHN W. HENDERSON, M.D.
Rochester, Minnesota

Among the bilateral afflictions of the so-called external eye is a fairly well-known but little recognized condition involving the lacrimal gland, the surface of the cornea, and the surface of the conjunctiva. The medium through which such an unusual association of pathologic conditions of the tissue comes about is the common tear. As with other bodily secretions and specialized tissues that are concerned with the everyday protection of our organs from harmful external agents, a normal supply of tears is taken for granted. When, for some unknown reason, the lacrimal gland does not provide us with a normal quantity of tears we are indeed puzzled as to what brought about such an unusual event. In the search for a better understanding of this phenomenon most attention has been directed to the changes that occur on the surface of the eyeball as a result of the alteration in tear supply, and descriptive terms have been proposed to differentiate this condition from other diseases of the eye.

The term "keratoconjunctivitis sicca," which was introduced into general use by Sjøgren,[1-12] literally means "an inflammation of the cornea and conjunctiva associated with dryness." Duke-Elder[13] referred to this same eye disease simply as "keratitis sicca." In English-speaking countries "keratitis sicca" has become the more widely used term, for it is in the cornea that several of the cardinal signs of the disease are to be found. However, the conjunctiva is also extensively involved, although the changes are not as evident as in the cornea unless a suitable dye is applied topically. Sjøgren's term is the more inclusive and more properly defines the disease in question.

A review of the subject matter was undertaken in an attempt to clarify the baffling systemic manifestations that are said to be associated with the ophthalmic condition. In addition a large series of cases were studied in the hope that a better knowledge of the ocular condition would be acquired.

HISTORY

It is interesting to delve into the historical background of this ophthalmic condition and learn of the earlier observations and evolution of thought concerning the disease process. "Filaments," an alteration of the corneal epithelium that is now known to occur in some types of keratoconjunctivitis sicca, were described by Leber[14] in 1882 as the diagnostic feature of filamentary keratitis. However, Leber and others (Uhthoff[15] and Fischer[16]), who observed this condition for the first time, did not recognize the exact nature of the filaments. Roeder,[17] as well as Hess,[18, 19] pointed out the epithelial origin of the threadlike formations attached to the surface of the cornea.

In spite of these observations and the extensive investigations of the physiology of the lacrimal gland published by Schirmer[20] in 1903, the association of filamentary keratitis with an alteration in the secretion from the lacrimal gland was not noted.

Fuchs,[21] in 1919, in his report of a woman, aged 54 years, with dry-appearing conjunctivas and diminished lacrimal secretion, seems to have been the first to record such a relationship. Fuchs also noted a diminution of salivary secretion and enlargement of the parotid glands in the same case.

In 1924, Stock,[22] director of the ophthalmologic clinic in Tübingen, called attention to diminution of tear secretion as one of the causes of filamentary keratitis. It was his be-

* From the Section on Ophthalmology, Mayo Clinic.

lief that this ophthalmic disease occurred mainly in women of the climacteric age. Stock stimulated the interest of others in his clinic. Schöninger,[23] an assistant in Stock's clinic, reported a woman afflicted with filamentary keratitis, aged 42 years, who had been unable to weep since the age of 18 years.

Mulock Houwer,[24] in 1927, stressed the frequent association of "keratitis filamentosa" with arthritis (this relationship was first recorded by Fischer[16] in 1889 in a single case) and reported 10 cases. In 2 of these 10 cases the patients were men, Mulock Houwer apparently having been one of the first to note the occurrence of this particular ophthalmic disease in other than the female sex.

In 1928, Betsch,[25] also an assistant in Stock's clinic, observed that a certain type of stippling of the corneal epithelium preceded the formation of threads or filaments, the latter appearing only when the ophthalmic disease reached a climax. Betsch, then, was apparently one of the first to imply that changes in the eye other than filamentary keratitis were associated with an alteration in the secretions of the lacrimal gland. In one patient of the two on whom Betsch reported, hoarseness, dry mouth, and atrophic rhinitis were noted. Betsch further implicated an endocrine relationship to the ophthalmic disease when he noted that the pharyngeal and ophthalmic symptoms seemed to abate regularly with the onset of menses.

In the same year, 1928, the first microscopic examinations of the lacrimal glands obtained from patients suffering from filamentary keratitis associated with alteration of tear secretions were made by Albrich[26] in three cases. Between 1928 and 1931, five more case reports appeared in the literature; the relationship between the ophthalmic disease and arthritis again being noted by Isakowitz,[27] and endocrine cause being suggested by Scheerer[28] and by Hauer,[29] and an altered sweat secretion in one case being discovered by Isakowitz.

By the year 1931, then, it was known that a certain type of ophthalmic disease affecting chiefly the cornea could be produced by an alteration of tear secretion secondary to changes in the lacrimal glands. The disease was known to affect both eyes, seemed to be linked to the female sex, and was thought to be produced by a diminution or absence of tears. The exact mechanism responsible for the changes in the lacrimal glands was not known. Furthermore a similar process affecting other mucous membranes was known to occur and endocrine disturbances were conjectured. All of the cases had been observed on the European continent and practically all of the reports, with the exception of Mulock Houwer's[24] paper, given before the Ophthalmological Society of the United Kingdom, were made in the German language.

In January, 1930, Sjøgren,[1] of Sweden, observed his first case of filamentary keratitis associated with deficient tear secretion. He became keenly interested in this ophthalmic disease and his writings, observations and research have stimulated ophthalmologists to recognize and study the disease. Just 16 years ago, in 1933, Sjøgren[1] first published the results of his three-year study. In this initial report he recorded 19 cases, the largest total to be observed by one man up to this time. Between 1933 and 1941, Sjøgren published a total of 10 reports on different aspects of the disease. By 1940 he had collected data on 50 cases, one of the largest series to be recorded to date. It was Sjøgren who pointed out that the conjunctiva was as frequently affected as the cornea and, as indicated in an earlier paragraph, he proposed the term "keratoconjunctivitis sicca."

Sjøgren revived and introduced into general use Schirmer's[30] method of measuring the secretion of tears. Sjøgren also detailed the clinical signs and symptoms of the disease and made comprehensive studies of the pathologic features occurring in the conjunctiva, cornea, lacrimal, and salivary

glands. He followed his patients over a sufficient period to recognize the occurrence of remissions and exacerbations. In short, his observations were so complete that little additional knowledge has been gained in the nine years since his last report. On some features of the disease, notably its sex incidence, Sjøgren changed his opinion between the times of his first and last report.

Sjøgren carefully scrutinized his patients for other systemic disorders, for he felt that the ophthalmic disease was often part of a symptom complex. In his 1933 report, he established the frequent association of deficient lacrimal secretion with deficient salivary secretion and enlargement of the parotid glands. These clinical features seemed to occur sufficiently often to constitute a syndrome. In his summary in 1940 in Ridley and Sorsby's text,[12] this syndrome had come to include keratoconjunctivitis sicca, xerostomia, laryngitis sicca, rhinitis sicca, pharyngitis sicca, enlargement of the parotid glands and chronic polyarthritis. When two or more of these conditions occur in the same person the symptom complex has come to be known, by common usage, as Sjøgren's syndrome, although Sjøgren[11] proposed the the term "dacryosialoadenopathia atrophicans."

Most of Sjøgren's reports were recorded in Swedish journals. With the publication of the second volume of Duke-Elder's[12] *Textbook of Ophthalmology* in 1941 this ophthalmic disease became familiar to English-speaking ophthalmologists as "keratitis sicca." The contribution of Beetham[30] in 1935 relative to a method of treating the ophthalmic difficulty, the excellent review of the subject matter by Bruce[31] in 1941, and the careful translation of Sjøgren's original article[1] by Hamilton which was circulated as a monograph, have brought the ophthalmic disease and its associated symptoms more forcibly to the attention of ophthalmologists in the United States. Subsequent reports by Gifford and associates[32] and by de Roetth[33, 34] have suggested that keratoconjunctivitis sicca is only one phase of a fundamental disturbance in the secretion of the lacrimal glands. These reports represent the most recent comprehensive data on the subject.

General considerations

Keratoconjunctivitis sicca as a disease associated with an altered production of tears has been known for approximately 30 years. Information concerning this condition can be gleaned from published reports of cases, from reports of Sjøgren's syndrome, or from discussions concerning hypofunction of the lacrimal glands.

From the reports made by Albrich,[20] Andersen,[35] Bach,[36] Betsch,[23] Beetham,[30] Bruce,[31] de Roetth,[33, 34] Franceschetti,[37] Fried and Goldzieher,[38] Fuchs,[21] Gifford and associates,[32] Godtfredsen,[39] Grósz,[40] Hamilton,[41] Hansen,[42] Hauer,[29] Muloch Houwer,[24] Isakowitz,[27] Krasso,[43] Leriche,[44] Lisch,[45] Lutman and Favata,[46] MacLean,[47] Riva,[48] Rucker,[49, 50] Scheerer,[26] Schöninger,[25] Sjøgren,[1-12] Spector,[51] Stahel,[52] Stenstam,[53] Vogt,[54] Weber and Schlüter,[55] Wissman,[56] and Ytrehus,[57] data on a total of 280 cases were collected.

References to this ophthalmic disease also were made in the articles of Bossalino,[58] the Dalsgaard-Nielsens,[59] Iversen,[60] Medunina,[61] and Mørch,[62] but it was not possible to determine the number of cases covered by their observations because their reports were not available to me for direct examination. Making a liberal allowance for the cases probably covered in the publications by the latter group plus some undiscovered reports probably tucked away in the literature, there are probably no more than 300 cases on record.

This number of cases would seem to be an adequate coverage of the subject considering the 30-year period and the number of observers who have written about the disease, except that the majority of the reports concern only a relatively few cases. Fifty-five percent of the 280 cases were cov-

ered in reports by Sjøgren (50 cases), Stenstam (47 cases), Gifford and associates (33 cases), and Godtfredsen (23 cases). Thus the opportunity to study this disease extensively has been the privilege of relatively few of the observers.

If we base our knowledge of this disease on the conclusions reached by the numerous observers reporting single or relatively few cases, we find that there are more systemic ramifications of the ophthalmic disease than would be reasonably expected.

In many instances the conclusions reached by observation of a larger series of cases differed from the data obtained from a study of a smaller number of cases. By a study of all the recorded cases supplemented by a large series from the files of the Mayo Clinic it was hoped that a better over-all picture of this interesting eye condition would be obtained.

Changes occurring in the cornea and conjunctiva similar to those noted in keratoconjunctivitis sicca are prone to occur after extirpation of a lacrimal gland;[63-66] after skull fractures wherein there has been damage to the nerve supply of a lacrimal gland;[63] as the result of a disturbance of the fifth cranial nerve[67] either by trauma or by herpes, or in instances in which there is a congenital absence of a lacrimal gland.[68] Such cases with a more obvious explanation of the ophthalmic difficulty were not included in this survey and review.

Our own cases that seemed to fulfill the criteria of keratoconjunctivitis sicca were collected from our files during the nine-year period 1938 through 1946. One hundred and twenty-one cases were obtained for study.

In all of these patients the manifestations of the ophthalmic disease were bilateral. Erosions or filaments of the corneal epithelium were present in all cases and in the majority of them slitlamp examination of the corneas was necessary to detect these alterations.

A diminution in the secretion of tears was another criterion on the basis of which these cases were diagnosed. The filter-paper test patterned after Schirmer's[20] Method I was utilized for determining the flow of tears. Schirmer's standard of less than 15 mm. wetting of the length of the filter paper strip in five minutes was accepted as indicating a deficiency in tear production for purposes of classification and diagnosis. On occasion patients were encountered who possessed a low tear flow, yet did not show alteration of the corneal epithelium. Such patients were not included in this survey.

Incidence

Although this ophthalmic disease has been noted by many observers, figures as to its frequency are strikingly absent. Sjøgren,[1] in one of his first papers, estimated its incidence to be 1 in 2,000 ophthalmic cases.

Beetham[30] in his thesis concerning filamentary keratitis also commented on the incidence of this disease. Although referred to as filamentary keratitis, Beetham's[30] cases were akin to those published by Sjøgren[1] as examples of keratoconjunctivitis sicca. In Beetham's series of ophthalmic patients from the Massachusetts Eye and Ear Infirmary, filamentary keratitis was estimated to occur once in 20,000 cases. Beetham naturally wondered if this disease were 10 times as frequent in Europe as in America. He concluded, and I think rightly, that observers in this country had failed to recognize the disease.

Gifford, Puntenney and Bellows,[32] in 1943, were the next to record a sizable number of cases. Over a four-year period they collected from their busy practice data on 49 patients with deficient lacrimation. Of these 49 patients, 33 were persons with keratoconjunctivitis sicca as the disease has been defined in a previous paragraph. Gifford and his colleagues, therefore, were seeing between 8 and 9 cases of this condition per year. This would indicate that the disease was being recognized more often, since Sjøgren's[1-12] cases were collected over the 10-year period 1930 to 1939.

A. de Roetth,[24] who has been very interested in the problem of keratoconjunctivitis sicca and has been on the lookout for such cases, commented on the incidence of this disease in his paper published in 1945. On the basis of 6,200 persons whom he had observed during the routine of his practice of ophthalmology he estimated the over-all incidence of persons with hypofunction of the lacrimal glands to be 1 in 200. Among these 6,200 patients there were 10 who presented the corneal changes along with the deficient secretion of tears that were typical of "keratitis sicca" and "filamentary keratitis." This would make an incidence of 1 in 620 cases.

On the basis of 121 cases collected from our files in a nine-year period, my colleagues and I are encountering between 13 and 14 patients with this disease per year. Because our observation of patients in the Section on Ophthalmology at the Mayo Clinic cannot be said to represent a routine eye practice and because a measurement of tear secretion and slitlamp examination of the cornea have not been routine with all patients, I do not feel a statistical estimation of the incidence of this disease is possible from our series. Even though we have collected data on a large series of these cases, I am sure that we have overlooked many examples of this disease.

De Roetth's[24] observations seem to be the most complete of any reports so far published on this phase of the problem, and in my opinion his figures most nearly approach the true incidence of this ophthalmic disease.

Sex

Throughout the evolution of the reports of keratoconjunctivitis sicca it had been observed almost exclusively in women. So definitely has the disease been associated with the female sex that many investigators have postulated an etiologic basis of a disturbance of the female hormones. Because the large series of cases covered by Sjøgren[1, 2, 5–7] in his earlier reports were confined exclusively to the female sex, some of the subsequent observers assumed that the disease did not occur in men.

Mulock Houwer,[34] in 1927, seems to have been the first to record the occurrence of the disease among men. Sjøgren was aware of Mulock Houwer's report when he made his initial contribution of data on 19 cases to the literature, but he commented on the arthritic aspects of Mulock Houwer's cases rather than the sex incidence. In 1937, Sjøgren[7] observed his first male patient, and in his discussion of the disease in Ridley and Sorsby's text[32] he noted that there were two men among the series of patients, who had by this time increased to 50.

Among the reports in the literature that I was able to examine I found the over-all sex incidence to be 94 percent female and 6 percent male. This figure does not include Stenstam's[33] recent observations. Stenstam seemed primarily interested in cases of rheumatoid arthritis. Among his cases of arthritis he noted 47 patients with keratoconjunctivitis sicca. He made the startling observation that men were as often affected as women. This observation is in marked variance to any other report concerning sex incidence. If Stenstam's observations are included in the estimation of the over-all sex distribution among the cases reported in the literature, the incidence of the disease among men would more nearly approach 14 percent; in women 86 percent.

In the series of 121 cases from the Mayo Clinic 17 (14 percent) patients were male and 104 (86 percent) were female.

It would seem, then, that the disease is definitely associated with both sexes. Its predominance among women poses an interesting problem. Although our figures as to the incidence of the disease among men are higher than any other published report except that of Stenstam, I feel that the incidence among men may be even higher than 14 percent. This is because the disease tends to be less severe in the male sex and such cases probably are overlooked more often.

Age

The evolution of thought concerning an age distribution has been intimately associated with the frequent occurrence of the disease among women. In so many of the cases, particularly among the earlier reports, the disease was observed among women who were passing through the menopause. It was natural, then, to deduce that the onset of the menopause played some part in the onset of the symptoms and, furthermore, that the disease would probably be seen only in women between 40 and 50 years of age.

In 1930 Duke-Elder[68] referred to the condition as "occurring spontaneously in women after the climacteric" and again[13] in 1941 the typical picture of the disease was said to develop "soon after menstruation has ceased."

This concept has continued to crop up among reports and discussions of the condition. In 1940, Sjøgren[12] reiterated his belief that the disease was limited almost exclusively to women more than 40 years of age (Sjøgren,[11,12] "age group 40 to 65" years) but had come to believe that the disease had no connection with the menopause.

From the reports of Bruce,[21] Gifford and associates,[22] Lutman and Favata,[46] and Ytrehus,[37] there seems ample evidence that symptoms occur before the menopause, a fact which would substantiate the opinions of those who contend that either the disease has no relationship to the menopause or the association is coincidental. At one extreme of the age scale is the 17-year-old girl reported by Rucker[49] and at the other extreme are the 12 women reported by Franceschetti,[27] the youngest of whom was 60 years of age.

The age spread among the 33 ("group II and group III") patients of Gifford and associates[22] ranged from 29 to 77 years and the average age of these patients at the time they were examined was calculated to be 54 years.

It is of interest, then, to delve into the age distribution of the 121 patients from our files. Among the women the youngest was 19 years of age and the oldest was 74 years. Among the men the youngest was 22 years and the oldest was 74 years of age. In Table 1 the age distribution among women is given.

From this tabulation one can readily see that symptoms are more likely to develop between 40 and 60 years than at any other age, but actually the patients in this age group only make up 50 percent (53 of 104) of the total. In 36 percent of the total, symptoms developed before the onset of the menopause. These data indicate that the disease among women occurs chiefly between the ages of 30 and 70 years and further imply that the menopause has little to do with the onset of symptoms of this disease.

TABLE 1

AGE DISTRIBUTION OF WOMEN WHO HAVE KERATOCONJUNCTIVITIS SICCA

Age at onset of Symptoms (years)	Women affected
Younger than 30	5
30–39	22
40–49	27
50–59	26
60–69	20
70 and older	4

Among the 17 men there was an age distribution similar to that tabulated for the women. The average age at the time of onset of symptoms was 47.1 years among the men.

Symptomatology

The symptoms of this disease have been listed among the reports of Beetham,[20] Bruce,[21] Gifford and associates,[22] and Sjøgren.[1,2,5,7,12] The symptoms referable to the eyes that bring the patient to the ophthalmologist were noted but, with the exception of Sjøgren's reports, not much emphasis has been placed on how these symptoms either compare with, or differ from, the symptoms of other ophthalmic diseases. Around the patient's so-called presenting complaints re-

volves the problem of why so many of these cases are probably overlooked. If ophthalmologists were more familiar with the subjective symptom complex, the measurement of the tear secretion and an examination of the cornea and conjunctiva with the slitlamp, which are the tests necessary to clinch a diagnosis, would be performed more frequently.

Patients afflicted with this disease are likely to describe their eyes as being "sensitive to light," "dry," and "red"; to call one's attention to an excess of "sticky discharge"; to note sensations of "burning," "itching," "smarting" and "scratching"; or to relate that they have "ulcers" and an inability "to cry or weep." In addition they may state that their eyes are "tired" or "irritable" and may refer vaguely to "soreness" and "pain."

With this maze of complaints one may question whether there is a typical symptomatology. It is true that many of these symptoms are common to other conditions such as blepharitis, chronic conjunctivitis, foreign bodies in the conjunctiva or cornea, and the asthenopia associated with uncorrected errors of refraction. However, two or three of these symptoms are so often a part of the patient's story that an underlying keratoconjunctivitis sicca should be suspected if the more obvious eye diseases are excluded.

In our series of cases the patient's statements were tabulated in an attempt to learn what the usual story might be. In Table 2 the symptoms are listed according to their relative frequency.

The symptoms of "burning" and "smarting" were so often interchangeable in the patient's mind that I have considered them to represent one and the same symptom. As noted in Table 2 this is more frequently encountered than any other single symptom. It is a symptom that is not often heard in the history given by patients afflicted with other diseases of the external eye. When it occurs, particularly among women, one should suspect keratoconjunctivitis sicca until proved otherwise. I have also run across this symptom among persons who exhibit a diminished secretion of tears but who do not show visible changes in either the conjunctiva or cornea. De Roetth[33] has also noted this association, and I agree that these people represent potential cases of keratoconjunctivitis sicca. The complaint of burning, then, may either indicate the presence of this disease of the eyes or serve as a premonitory symptom.

Scratching or a sensation of "something in the eye" was the next most frequent single symptom. This complaint as a symptom of keratoconjunctivitis sicca did not seem to have any characteristics that would help to differentiate it from similar symptoms resulting from other diseases of the eye. A roughening or ulceration of the surface of the conjunctiva or cornea probably is the basis for this symptom. When this symptom occurs, the eye disease is moderately advanced in degree.

TABLE 2

FREQUENCY OF SYMPTOMS

Presenting symptoms	Frequency (percent)
Burning and smarting	16
Scratching and foreign body sensation	13
Excess of secretion	12
Dryness	11
Redness	9
Photosensitivity	6
Itching	5
Inability to cry or lack of tears	3
Diminished vision	1
Ulcers	1
Tiring, irritability, hurting, soreness, pain	23

The "mucous" discharge which annoys these patients is often referred to as being "ropy," "stringy," "tough," or "hard." When patients wipe away a yellow, inspissated, tenacious mass of secretion from the region of the inner canthus or peel out with their fingernails from the lower fornix of the conjunctival sac a ropy threadlike mass of whitish secretion, one cannot help being impressed by the possible diagnostic significance

of the patient's mannerism. In no other common disease of the eyes except in vernal conjunctivitis are the patients so anxious to rid themselves of the secretions or so prone to exhibit to the observer the cause of their complaint. As a rule this symptom is not encountered except in cases of moderate severity and the secretion from the eyes becomes more annoying as the disease progresses.

"Dryness" or the sensation of the eye being "dry" is an excellent clue to the nature of the underlying ophthalmic disease. In no other disease of the eyes is this symptom so likely to be mentioned as in keratoconjunctivitis sicca. Unfortunately this symptom does not occur as frequently as some of the other symptoms, for a diagnosis of the disease might more readily be made on the basis of this one symptom than on any other single complaint. Paradoxically the patients may say that their eyes are dry; yet the eyes themselves may appear moist.

"Redness" or the tendency of the eyes "to get red" is neither as frequent nor as constant a complaint as are many of the other symptoms of this disease. If redness is one of the presenting symptoms, the patient will often add that "the eyes are red only part of the time" and, vice versa, if this symptom is not mentioned the patients will admit on direct questioning that "the eyes are sometimes red." To the patient "redness" means a congestion of the bulbar conjunctiva and, as will be mentioned later, this symptom may not be as likely the result of keratoconjunctivitis sicca as of some infection that is superimposed.

A sensitivity to light or an intolerance of glare is mentioned often enough to be included in a tabulation of the symptoms of this disease. This symptom should draw attention to the cornea. If keratitis is obviously absent on gross inspection of the eye, the cornea should be studied with slitlamp for the stippling and filamentary characteristics of the disease. The vagaries of this symptom are puzzling. I have encountered it among very mild examples of the disease and have noted its absence among cases of severe degree where its occurrence would reasonably be expected. As a clue to keratoconjunctivitis sicca, photosensitivity is not very helpful. Although this photosensitivity can become a photophobia and be very discomforting, I have not seen a case as severe as the one reported by Sjøgren[1] wherein the photophobia was so marked that it was necessary for the patient to keep her head buried in the pillow.

"Itching" of the eyes is so infrequently encountered that it cannot be relied on to furnish much help in diagnosing the disease. When present, this symptom is usually associated with an inability to rid the conjunctiva of the annoying tenacious secretion that accumulates in the severer forms of the disease.

A statement of an inability to weep or a lack of tears is seldom volunteered by the patient. Patients who have been correctly diagnosed elsewhere will usually mention this symptom and persons who suffer from a severe and chronic form of the disease will soon associate their difficulties with a diminished supply of tears.

A decrease in visual acuity will be referred to by the patient simply as "blurred vision." It is not a part of the symptom complex until the disease has reached such a stage that the central area of the cornea is affected by "epithelial filaments" or erosions. By this time the disease should be so obvious that reliance on the symptomatology as an aid to the discovery of the disease will not be necessary.

"Ulcers," to the patients afflicted with this disease of the eyes, connote a condition that has been discovered by some other ophthalmologist during the course of a slitlamp examination. As a symptom it should make the observer aware of the possibility of keratoconjunctivitis sicca.

Last in the series of symptoms listed in Table 2 are a number of symptoms that by themselves have little or no significance but,

when occurring in combinations of two or more, as they sometimes do in cases of keratoconjunctivitis sicca, they constitute the most frequent symptom complex of this disease.

It is unfortunate that these symptoms are so often vague, for they offer no definite clue as to the underlying difficulty. Patients with these combinations of symptoms are the ones in whom the disease is so often overlooked. The fact that these patients have received so many pairs of spectacles and have been treated by so many ophthalmologists should make one aware that if an organic basis for the complaint exists it will be something out of the ordinary. As a rule patients presenting this symptom complex exhibit only the milder forms of the disease, so that the condition is more of an annoyance than a disability.

In addition to the descriptive adjectives that these patients use to report their difficulties, they sometimes make statements referable to factors which aggravate their symptoms. The increase in the severity of their difficulties brought on by reading is one such factor. So far as the symptomatology of keratoconjunctivitis sicca is concerned this factor has no special significance because this complaint is common to many eye conditions. However, when patients state that their symptoms are usually worse when awakening than at other times, then one should consider the possibility of this disease.

Often these patients will describe a tight feeling in the eyelids and say that it is "difficult to open the eyes." The lack of lubricant between the surface of the eyeball and the conjunctival surface of the eyelids is probably responsible for this symptom. When the act of opening the eyes after sleep is actually accompanied by sharp pain, then there is probably a peeling away of the superficial epithelium of the cornea as the eyeball is rotated downward to its position of attention.

In general, then, it cannot be said that a typical subjective complex of symptoms exists for keratoconjunctivitis sicca. The ophthalmologist must still rely on a measurement of the tear secretion and a study of the cornea and conjunctiva with the slitlamp to enable him to make the diagnosis. However, certain symptoms such as dryness, burning or smarting, scratching, and excess of a typical mucoid secretion occur frequently enough (52 percent of the cases) to warn the examiner as to the presence of this disease.

Clinical signs

The onset of this disease is so insidious that it is difficult for many patients to date their initial symptoms. This was particularly evident among the male patients of our series. Women in the 20-year to 45-year age group are likely to associate the initial signs and symptoms with the onset of pregnancy or the birth of a child. Older women may date the onset to some gynecologic operation.

In the majority of instances the evolution of signs and symptoms is so slow and intermittent that some months or years may elapse before the person decides that a definite ophthalmic difficulty exists. During this stage of evolution, the ocular symptoms may be only an annoyance or nuisance to the patient and definite signs of the disease either are not present or are difficult to demonstrate. Once the clinical course has progressed to such a degree as to be classified as keratoconjunctivitis sicca certain signs are present which definitely establish a diagnosis.

A definite sign, although variable in degree, is a diminution in the production of tears. For determining this manifestation one of the methods evolved by Shirmer[20] has been universally utilized. Schirmer employed strips of filter paper, 5 mm. wide and 35 mm. in length. A right-angle fold was made in the filter paper 5 mm. from one end so that the strip could be hung over the lower lid, the short end of the strip approximating the surface of the palpebral conjunctiva and the remainder of the strip protruding from the eyelid.

Schirmer placed the strip near the external canthus and allowed the patient to keep the eyelids open during the five-minute duration of the test. During the passage of the years since Schirmer's work, the test has been modified in various ways to include placing the strips of filter paper over the lower lacrimal puncta, using paper other than the filter type and conducting the test with the eyelids closed. In spite of these attempted refinements the basic features of Schirmer's method have been retained and are still employed at the present time.

Schirmer tested more than 100 persons and decided that a wetting of the filter paper of less than 15 mm. in five minutes indicated a deficiency in the secretion of tears. Sjögren[3] accepted Schirmer's figures as the upper limit of normal in his investigations, and Gifford and associates[32] utilized the same numerical value in their classification of persons with deficient lacrimation.

Gifford and associates, Beetham,[20] and de Roetth[34] have all observed people with less than 15 mm. of wetting in five minutes who either were normal in all other respects or did not exhibit any of the other signs of keratoconjunctivitis sicca. These observations prompted Beetham to establish as his lower limits of normal a wetting of 10 mm. in five minutes.

De Roetth, who examined the tear secretion in 162 persons by the method of Schirmer, found that a third of the persons more than 40 years of age exhibited a wetting of 15 mm. or less in five minutes. He stated that a production of less than 4 mm. was usually accompanied by subjective symptoms and that it was exceptional to find symptoms of lacrimal deficiency when more than 10 mm. of wetting in five minutes was present.

It is difficult to be dogmatic as to the limits of normal, for there is a personal variation in the conduct and interpretation of the test and the absorbability of the testing agent may vary. De Roetth,[34] after a study of several types of paper, recommended double acid-washed, Whatman No. 41 filter paper. Furthermore not many investigations have been carried out on the measurement of the tear secretion by this method among men and women of different age groups.

Schirmer, in terms of definite quantity, estimated the output of tears as 0.5 to 0.67 gm. per day under normal conditions but stated that younger persons have more tears than older people. De Roetth[33] also noted the decrease of tear production with age and further noted that young women have a more active lacrimation than young men; whereas, older women produce a lesser amount of tears than older men. A further attempt to elucidate this problem is being carried out on a series of our own patients.[69]

Further imperfections exist in determining the presence of this sign in this disease when it is realized that the filter paper in contact with the conjunctiva may serve as an irritant and in so doing call forth a greater production of tears than exists under other circumstances. In addition, the tear secretion is likely to vary from day to day even among the patients with well-established keratoconjunctivitis sicca, so that in borderline cases a series of determinations should be averaged.

Many other observers have pointed out the fact that the Schirmer test in reality measures only the secretion present in the conjunctival sac at any given time and is not a direct and true measurement of the secretion of the lacrimal gland, since the secretion from the mucous glands of the conjunctiva may augment the reading.

Each observer, then, must be aware of these factors when investigations for this disease are carried out and must establish a normal for the technique and filter paper which is employed. Regardless of the objections to the method proposed by Schirmer,[20] it is still the most practical test for determining one of the important signs of this disease. Finally, it must be remembered that a diagnosis should not be made on the basis of this test alone.

The most important clinical features of keratoconjunctivitis sicca are to be found in the corneas. The changes that occur in these tissues of the eyes are characteristic and when associated with a diminution of tears are diagnostic of the disease. Unfortunately, from the standpoint of ready diagnosis, these changes are not visible unless the eyes are examined with the slitlamp and binocular loupe. In general, three types of alterations may be found: minute breaks in the surface of the cornea, gray foci of various shapes and size, and threadlike filaments. These modifications are usually confined to the epithelial layer of the cornea and even with the aid of the slitlamp and binocular loupe they are not easily seen unless a suitable dye is instilled.

A weak solution of fluorescein seems to be the most suitable dye for staining purposes. The minute breaks in the epithelium readily accept the stain and appear as bright-green, punctate defects. When numerous, these superficial erosions give a stippled appearance to the corneal epithelium. They are usually discrete but may be confluent, and the picture is akin to that described as superficial punctate keratitis.

The foci of infiltration do not accept the stain as readily as the erosions and therefore appear a dull gray-green color. They are a little larger in diameter than the erosions and are discrete. Sometimes they are visible in the superficial layers of the substantia propria as well as the epithelium.

The threadlike filaments are seen to be rolls of epithelium that hang from the surface of the cornea and are attached at one end. They may vary from a fraction of a millimeter to several millimeters in length and also accept the fluorescein dye. These threads are identical with those described in the various types of filamentary keratitis.

Characteristically these alterations of the corneal surface are bilateral but may be unequal in degree and cannot be said to be exactly symmetrical. For the most part the damage exhibited by each cornea is sufficiently alike to justify one in saying that the eyes are equally affected by the progress of the disease.

From a study of the patients in our series, it would seem that the erosions and punctate staining areas represent the earliest effects of the disease on the cornea. As the severity of the disease progresses, these staining areas will increase in number and between them the foci of infiltration will appear. As the disease reaches its climax the filaments will appear, so that all three types of alterations in the surface of the cornea will be visible.

In the initial and moderately advanced stages of the disease, only the lower third of the cornea will be likely to exhibit these changes, but when the disease nears its final stage the entire surface of the cornea will be covered by filaments. When such an event occurs, the corneal reflex will be dull, a hypesthesia may exist, and the visual acuity will be reduced. Until the final climax there will be little evidence, from the standpoint of vision and the gross appearance of the corneas, that a disease of the corneas exists.

Of the two main features of this disease, the diminution of tears and the modifications in the corneal epithelium, it is on the basis of the latter that the severity or progress of the disease is probably best judged. As a rule the diminution of tears, as measured by the Schirmer test, roughly parallels the increasing damage to the corneas, but so frequently have I observed a low tear secretion in eyes otherwise asymptomatic and free of objective signs and, vice versa, a relatively good secretion in eyes with badly affected corneas, that I have come to look on the values of the Schirmer test as unreliable in prediction of the severity of the disease. In some instances, the more severely affected eye has possessed a seemingly better tear supply than the apparently less affected fellow eye.

The epithelium of the cornea is not the only surface tissue that is affected; the conjunctival surfaces of the eyeball and the eyelids share in the disease process too. How-

ever, the changes in the conjunctiva are even more difficult to visualize clinically than those in the corneas. The sclera and tarsal plates are not suitable backgrounds to offer a contrast for the changes occurring on the surface of the conjunctiva, and the conjunctival epithelium does not seem to accept fluorescein dye as readily as the epithelium of the cornea.

It was Schirmer[7] who introduced the dye, bengal rose, as the most suitable agent for showing these changes. When a one-percent solution of this dye is introduced into the conjunctival sac of a person afflicted with this disease that portion of the bulbar conjunctiva roughly corresponding to the palpebral apertures will take on a reddish hue. The corresponding portions of the surface of the plica and caruncle will also accept the stain, indicating that these portions of the conjunctiva are also involved. The basis for this staining characteristic probably lies in the minute erosions of the epithelium of the conjunctiva, and the intensity of the stain is roughly proportional to the severity of the disease.

The staining with fluorescein is more patchy and less diffuse than with bengal rose. The more protected portion of the conjunctiva, such as covers the eyelids and is adjacent to the fornices, does not stain well with either dye.

Without the topical dyes there is very little to be seen when the conjunctiva is routinely examined. This probably accounts for the scant attention that is paid to the conjunctiva in many case reports of the disease.

Furthermore, even in severe cases, the conjunctiva always appears moist and gives no clue that desiccation or dryness may exist. At the most there will be visible dilated capillaries in the bulbar conjunctiva, and the lower palpebral conjunctiva may present a diffuse congestion of mild degree. Papillary hypertrophy of the conjunctiva and follicle formation are not characteristics of this disease. Pericorneal congestion is an inconstant feature and, when present, is usually associated with the more advanced changes in the cornea.

In most cases during some phase of the disease, the patient will note a more intense congestion of the eyes than is ordinarily present. Accompanying this congestion of the eyes will be an exacerbation of the patient's symptoms and a change in the character of the secretion from the conjunctiva. It is during these episodes that the patients will complain of their eyes being "red."

Inspection of the eyes may reveal a congestion of the bulbar and palpebral conjunctiva, a papillary hypertrophy of the palpebral conjunctiva of some degree, and a more mucopurulent appearance in the secretion that is wiped from the eyelids. In short, all of the changes of a conjunctivitis will be present except epiphora. I have come to regard these episodes as representing an invasion of the conjunctivas and corneas by pathogenic organisms rather than representing a phase in the progress of the keratoconjunctivitis sicca.

It would seem reasonable that the surface tissues of the eye, denied their normal protecting coat of tears, would be more susceptible to invading pathogens and even some organisms that would ordinarily be saprophytic. It is during these intermittent episodes of ocular discomfort that the patient is driven to seek medical treatment. The conjunctivitis will be diagnosed and an attempt made to treat it, but in the majority of cases the ophthalmologist will be unaware that the underlying and predisposing disease, keratoconjunctivitis sicca, is present.

In the discussion of the symptomatology of keratoconjunctivitis sicca attention was directed to the type of secretion that accompanies some phases of this disease. Some mention was made of the physical characteristics of this secretion, and it was pointed out that the secretion often seemed an annoyance to the patient.

In the more mild degrees of this disease, the gross appearance of the conjunctival secretion is not altered sufficiently to dif-

ferentiate it from the secretion observed in other ocular conditions such as chronic conjunctivitis. As the disease process progresses the character of the discharge is so altered as to serve as a clinical sign of this disease.

As the lower lid is depressed one will encounter strands of whitish gray material nestled amidst the folds of the conjunctiva in the lower fornix. If one attempts to extract this material, one will find it to be rather tenacious and ropy in consistency, a feature which likens it to the discharge encountered in cases of vernal conjunctivitis.

If stained with suitable dyes and examined under the microscope, the secretion will be found to consist chiefly of epithelial cells and mucus. A few diphtheroids or xerosis bacilli may also be found in the secretion.

On the surface of the eyeball the capillary film of fluid will be more viscid than normal, and flecks of mucus and small clumps of epithelial cells may sweep across the surface of the eyeball as the eyelids are blinked. As the secretion is swept to the area of the inner canthus during the normal process of winking, it will assume a more yellow color and become inspissated and hard in texture. This latter feature will be particularly noticeable in persons who are examined shortly after awakening from a nap or a night's sleep.

Although the lacrimal glands are among the tissues chiefly involved in the disease process, there is little to indicate their involvement from the standpoint of clinical inspection. There is no swelling or enlargement of the glands, and palpation of the upper lid in the region of the lacrimal fossa will not reveal any apparent changes in the consistency of the glandular tissue.

One of the puzzling clinical features of this disease is the tendency toward remissions. Not all of the cases will exhibit this feature, but in many of them there will be a temporary alleviation of symptoms and some of the clinical signs of the disease will disappear. At present it does not seem possible from the knowledge of this disease to predict, from the clinical findings alone, when the remissions will occur or how long they will last. The patient is likely to associate the remission with a feeling of well-being or an improvement in general health. During these intervals, as a rule, most of the annoying symptoms will subside, but a few staining areas will still be present if the surface of the cornea is meticulously inspected and some diminution of tears by Schirmer's test will persist.

Another interesting and closely related feature of the disease will be the apparent lack of progress in the severity of the signs and symptoms in some cases. In general, most observers believe the disease to be slowly progressive in its intensity, and for the most part this is probably true. In some of the cases in our series, the increase in the severity of the signs and symptoms has been so slight as almost to justify one in saying that the disease has reached a standstill. Gifford, Puntenney, and Bellows[82] observed some of their borderline cases of keratoconjunctivitis sicca for periods ranging from 6 to 12 months without noting signs of progress.

As part of the clinical manifestations of this condition, the infrequent occurrence of severe ocular complications should be noted. Sjøgren[1] in his first paper on the subject said that complications are never found, and other observers have repeated this statement.

The exacerbations of the disease and the severe episodes of conjunctivitis that I believe are often caused by a bacterial invasion of the conjunctiva (as noted in a previous paragraph) are probably the most frequent of the complications. In none of these situations that have come under my observation were there any permanent ocular sequelas directly attributable to keratoconjunctivitis sicca.

In some of the patients exhibiting the more severe involvements of the corneal epithelium, I have frequently noted tiny vascular loops, visible only with the aid of the slitlamp and binocular loupe, passing

across the limbus into the extreme periphery of the corneal stroma, but I should hesitate to classify such vascularization as a true pannus or complication.

Sjøgren[11] in one of his later papers noted a dense pannus form in one of his patients, and Bruce[31] observed the development of a dense corneal opacity in one of his cases. When such phenomena occur I should be suspicious that they represent the sequela of an intercurrent infection rather than a true complication of keratoconjunctivitis sicca.

It is amazing in some cases how the eye can be so devoid of tears and the cornea be so covered with filaments and yet suffer from so little permanent damage, for the visual acuity will improve and the cornea will resume a more normal appearance once moisture is restored by any therapeutic devices.

One other nonconstant feature in the clinical diagnosis of these cases should be mentioned. This is the tendency for many of the female patients to appear older than their stated age. Sjøgren[11] has noted this feature, too. Among our own series of patients, I have noted this apparent age change among the women in the fifth and sixth decades and among some of the younger women who are afflicted with a severe form of the disease.

Systemic manifestations

Reference has been made in previous paragraphs to the fact that keratoconjunctivitis sicca is often associated with symptoms and disorders referable to organs other than the eye. The exact relationship of the ophthalmic disease to certain other conditions occurring in the same person is one of the most interesting facets in the problem of keratoconjunctivitis sicca.

Chief credit for stimulating interest in this phase of the disease must go to Sjøgren. From the thorough analysis of each of his cases and his extensive publications on the subject a myriad of extraocular symptoms have come to be associated with the ophthalmic condition. The marked interest in the probable systemic ramifications of this disease created by Sjøgren's[1,2,3,6] earlier publications is reflected in the numerous subsequent discussions and reports of cases that have been published as examples of the syndrome that has come to be known by his name.

Almost every observer who has written on the subject has noted additional signs or symptoms that might represent examples of the syndrome. Of the 280 reports of cases of keratoconjunctivitis sicca in the literature that I was able to study about 86 percent concerned Sjøgren's syndrome.

This figure might lead one to assume that keratoconjunctivitis sicca as a single disease entity is relatively infrequent were it not for the possibility that many examples of the ophthalmic disease alone are overlooked and the fact that many additional symptoms, other than those defined by Sjøgren, are included in the reports of cases.

Among the many signs and symptoms observed by Sjøgren[1,2,3,6] in his earlier series of patients he noted that a dry mouth, dry nose, dry throat, hoarseness, and intermittent enlargement of the parotid glands were so frequently associated with dry eyes as to constitute a syndrome. By 1940, he had come to include chronic polyarthritis as part of the symptom complex.

Sjøgren[12] emphasized that not all of these components of the syndrome are likely to be encountered in any given case. He pointed out that if the disease progresses all of these symptoms may develop, but as a rule only 1 or 2 of the associated symptoms occur without a fixed order of appearance in the evolution of the disease. He recognized that keratoconjunctivitis sicca could occur without the other symptoms and correctly reasoned that the other components also could occur alone. He[12] further cautioned that to decide dogmatically on purely clinical evidence that any given symptom was a part of the syndrome was impossible unless a

histologic examination was performed.

In the study of the series of 121 patients seen at the Mayo Clinic I have considered that keratoconjunctivitis sicca, xerostomia, pharyngitis sicca, laryngitis sicca, rhinitis sicca, and enlargement of the parotid glands are the distinctive features of Sjøgren's syndrome. If the patient presented one or more of these conditions in association with keratoconjunctivitis sicca, the case was considered to be an example of Sjøgren's syndrome for the purposes of analysis. On strictly clinical grounds, as will be pointed out later, arthritis was not included in the symptom complex.

In our series of cases about 33 percent could be said to be definite examples of Sjøgren's syndrome, as defined in the foregoing paragraph. However, not all of our patients were directly questioned or minutely examined for extraocular symptoms and signs of Sjøgren's disease. Therefore, it would be reasonable to assume that in our own series the percentage of examples of Sjøgren's syndrome among the total number of cases of keratoconjunctivitis sicca would be higher than 33 percent.

Gifford, Puntenney, and Bellows,[32] who have reported one of the largest series (33 cases) of patients appearing in the American literature in whom the conjunctival and corneal changes of keratoconjunctivitis sicca were present, found that 36 percent (12 of 33) of their patients were examples of Sjøgren's syndrome. This latter value closely approaches the percentage figure reached by analysis of our own cases. Attention has already been directed to the high incidence (about 80 percent) of Sjøgren's syndrome among the cases of keratoconjunctivitis sicca reported in the literature.

It was of interest to compare the age and sex incidence of patients with Sjøgren's disease in our series with the incidence of these factors among the cases of keratoconjunctivitis sicca in the literature. It has been pointed out in a previous paragraph that keratoconjunctivitis sicca is a disease of both sexes, predominant (86 percent) among women, and mostly affecting women 30 to 70 years of age. Of the examples of Sjøgren's syndrome in our series, 92.5 percent were women and 7.5 percent were men (total of 40 cases). In Table 3 is given the age distribution among our female patients with Sjøgren's syndrome.

If the data of Table 1 and Table 3 were plotted on a graph, the resulting frequency curves would be very similar except for total number of patients involved. Thus, the women showing evidence of Sjøgren's syndrome are in the same age distribution as those with keratoconjunctivitis sicca. When these same cases of Sjøgren's disease were analyzed as to the order of onset of their symptoms, it was found that in about half the cases the ophthalmic symptoms represented the initial complaints; whereas, in the remaining 50 percent of the cases, extraocular symtoms marked the advent of the disease. It would seem, then, that Sjøgren's disease is not always a logical sequence in the progress of keratoconjunctivitis sicca, but rather may represent a disease entity of its own with a similar age and sex distribution.

TABLE 3

AGE DISTRIBUTION OF WOMEN WHO HAVE SJØGREN'S SYNDROME

Age at onset of Symptoms, (years)	Women affected
Younger than 30	1
30–40	8
40–50	10
50–60	10
60–70	8

With the exception of the enlargement of the parotid glands, all of the signs of Sjøgren's syndrome seem to have, as the basis for their symptomatology, an alteration or diminution of the secretory supply from the glands that supply the organ in question.

Of the extraocular signs of the disease, xerostomia seems to be the most frequent.

A diminution of the saliva secreted by the submaxillary and parotid glands seems to be chiefly responsible for the oral symptoms. Practically all of the patients with this sign of the disease refer to the disability simply as a dry mouth. All of these patients encounter some difficulty in masticating food, supplementing the saliva with frequent sips of water during the course of a meal.

The mucous membrane may become so dry as to result in the cracking or fissuring of the lips and tongue. The tongue usually appears more red than normal and may be furred and dry in appearance. In the cases that have come to my attention I have not observed an instance in which the tongue was smooth and shiny in appearance.

The symptomatology and appearance of the nose, throat, and larynx in this syndrome have received scant comment in the ear, nose, and throat publications. The nose and throat are often referred to by the patients as raw and dry. The pharynx will appear granular and congested in such cases. Hoarseness will reflect the changes that have occurred in the larynx.

It has not been possible to explain the enlargement of the parotid glands on the basis of the histologic studies that have been carried out, for the latter have shown essentially a process of fibrosis and atrophy. This swelling of the parotid glands is intermittent in its appearance and is usually self-limited, the glands returning to normal size in the patient's opinion. Several episodes of swelling may affect the same patient during the course of the disease. The frequent association of swelling with fever and local tenderness makes it likely that a secondary infection of the tubules of the gland, retrograde from the mouth, is responsible for these clinical features. The Dalsgaard-Nielsens[71] have also expressed this opinion as to the cause of the enlargement of the parotid glands.

The exact relationship of arthritis to the problem of keratoconjunctivitis sicca is a vexing one. Because symptoms of arthritis were so often noted among his patients and because arthritis may completely dominate the picture as the disease progresses, Sjøgren[11] included chronic polyarthritis as one of the features of the syndrome which he described. Sjøgren[11] was not certain that a distinctive type of arthritis formed this component of the syndrome, for he referred to some of his cases as exhibiting on roentgenologic examination "chronic infectious types" and to others as "endocrine types." The endocrine type of arthritis was originally described by Umber[72] as periarthritis destruens. Sjøgren's feeling that a more than casual relationship existed between chronic polyarthritis and the other signs of his syndrome was echoed in the publications subsequent to his time.

As to the frequency of arthritis among the cases of Sjøgren's syndrome, Beetham[20] noted it in 33 percent (3 of 9), Gifford and associates[32] in 58 percent (7 of 12), Godtfredsen[39] in 87 percent (20 of 23), Sjøgren[1] in 68 percent (13 of the 19 original cases), and MacLean[47] referred to a 60-percent incidence among all cases (exact number not stated) that he reviewed in the literature. The joints of the hands seemed to be the most frequently affected.

From these data and the opinions voiced by other writers on the subjects, it seems that chronic polyarthritis as a component of Sjøgren's syndrome has found general acceptance among ophthalmologists.

Just why there is a paucity of observations concerning this subject in the voluminous literature on arthritis is not clear, but strikingly, all of the foregoing data have been presented from the standpoint of the ophthalmologist. Stenstam[53] seems to be the only one who has investigated this problem from the standpoint of rheumatology. Among 495 patients with rheumatoid arthritis, he found that 47 patients (9.5 percent of the total) exhibited keratoconjunctivitis sicca. He came to the conclusion that it was unlikely that the arthritis was typical of or was a part of the ocular condition. He made another observation that seemed dia-

metrically opposed to the prevailing opinion up to this time when he noted that, among cases of keratoconjunctivitis sicca in his series, men and women were practically equally affected.

Of the 121 cases of keratoconjunctivitis sicca observed at the Mayo Clinic definite evidence of arthritis was collected in only 20 patients (17 percent of the total). This is about the lowest incidence that has been established among the studies in the literature that contain sufficient numbers of cases for statistical survey. In all fairness it should be pointed out that not all of the patients in our series were directly examined roentgenologically for evidence of arthritis if by history and physical examination there seemed to be no indication for special studies. The estimate of 17 percent might then be argued to be a bit low.

Among these 20 patients with arthritis a diagnosis of rheumatoid arthritis was made in 15 cases, senescent arthritis in one, mixed arthritis in one, and in three cases the arthritis could not be classified. Among the 40 cases of Sjøgren's syndrome in this series only 11 patients (27.5 percent) had arthritis. In both of these circumstances the relative incidence of arthritis seems too low to consider it a distinctive feature of keratoconjunctivitis sicca or an integral part of Sjøgren's syndrome in the series of patients that we have observed.

Sjøgren[5, 11] called attention to three other features that were often noted in the clinical study of his patients: lymphocytosis, elevated sedimentation rate, and "light grade" anemia. In general Sjøgren's observation of these particular clinical signs has not been noted sufficiently often by subsequent writers to consider them as typical findings in either keratoconjunctivitis sicca or cases of Sjøgren's disease.

Hypochromic anemia so often accompanies severe arthritis of any type that it would be difficult to relate it definitely to the ocular disease in question. An elevated sedimentation rate may also occur in the course of arthritis or it may reflect the secondary infection of the parotid glands rather than being a distinctive feature of either keratoconjunctivitis sicca or Sjøgren's syndrome.

Since the time when Fuchs[21] postulated some relationship to the female climacteric by the report of his case in 1919, there has been much evidence brought forward to link keratoconjunctivitis sicca with an endocrine disorder. Most of the evidence has been of a theoretical nature, however, and to date there is little practical proof that the ophthalmic disease and its extraocular manifestations are associated with symptoms of endocrine dysfunction. Because the disease has been observed almost exclusively in women by so many observers it was natural to assume that some endocrine disorder was also present.

Greatest attention has been directed toward the ovaries. Cases are on record wherein the conjunctival symptoms abated with the onset of the menses,[23] the disease seemed to subside with the termination of pregnancy,[28] and the onset of the disease followed an oophorectomy.[43] Numerous instances have been cited to show cause-and-effect relationship between the female climacteric and the onset of keratoconjunctivitis sicca.

De Roetth[34] cited some unpublished experimental observations of Hollas to show that dry corneas resulted only when the ovaries as well as the lacrimal glands were removed. To explain the presence of the disease among women who had not reached the age of the climacteric, de Roetth[34] also postulated some pathologic change in the ovaries.

The apparent success in the treatment of a patient over a three-year period with estrogens by Fried and Goldzieher[38] may be cited as additional evidence for a close tie-up between the endocrine glands and keratoconjunctivitis sicca.

One of the patients in our series reported a subsidence of the symptoms after hys-

terectomy. However, among the observers who believe in such a close relationship there is so great a disagreement as to the exact symptoms and signs of endocrine dysfunction that will occur, that it is impossible to accept this premise definitely. It must also be kept in mind that the disease is characterized by remissions, and that such remissions may be spontaneous rather than due to any apparent change in the hormonal balance of the person concerned.

Except for data which tend to refute the association of the disease with the female climacteric, as pointed out in a previous paragraph, analysis of our own series of cases sheds no further light on a possible endocrine relationship. In some of our cases we have tried to uncover symptoms or signs of an endocrine disturbance but to no avail.

In addition to the possible manifestations of this disease among organs other than the eye that have already been noted, a myriad of other symptoms have either been noted or discussed among the reports in the literature.

Changes in the skin (atypical scleroderma,[44] dry skin,[31] scleroderma of the cutis[73]); a loss of teeth;[1, 31, 34, 44, 46] enlargement of lymph glands;[20] blood dyscrasias (hemorrhagic purpura,[44] "peculiar" blood findings,[31] Felty's syndrome[37]); disturbances of the sympathetic nervous system;[44, 71] cyanosis of hands and feet;[31] achylia or subacidity;[1, 29, 45, 71, 74] vitamin deficiencies;[27, 29, 46, 52] alterations in serum protein,[29] and a diminution of sweating[1, 37] and their relationship to keratoconjunctivitis sicca have been noted.

If all of these clinical features were included as systemic manifestations of keratoconjunctivitis sicca, the ophthalmic disease truly would be a remarkable one. Furthermore, it would seem that the disease would be more widely recognized among the various medical specialties instead of being confined chiefly to the attention of ophthalmologists during the past 15 years.

A dryness of the skin and fingernails, an absence of sweating, a loss of teeth, especially among those with a dry mouth, Felty's syndrome, and avitaminosis A have occasionally been noted in isolated instances among cases of our own series, but in general I have come to regard the majority of these systemic features as of only casual or coincidental relationship to keratoconjunctivitis sicca.

Pathology

Albrich,[26] Beetham,[30] Sjøgren,[1, 12] Lutman and Favata,[46] all have made pathologic examinations of lacrimal glands obtained in cases of keratoconjunctivitis sicca. In addition, Sjøgren[1] has examined microscopically other tissues concerned in the syndrome of his name. Sjøgren's pathologic studies have been the most comprehensive, and the reader is referred to his two[1, 12] excellent discussions of the subject for the histologic details.

In general, Sjøgren[12] observed in the lacrimal glands a gradual disintegration of the gland tubules with replacement and infiltration by round cells. As the disease progresses the entire gland may be converted into scar tissue. Thus the process seems to be one of degeneration with final atrophy. A similar process occurs in the salivary glands and the mucous glands of the pharyngeal and laryngeal walls according to Sjøgren.

The most interesting changes seem to occur in the bulbar conjunctiva of affected patients. According to Sjøgren,[1] the earliest changes are those of an edema, as evidenced by the transudate found in the connective-tissue layer of the conjunctiva in early cases. If the edema increases, the fluid will penetrate into the epithelium, causing a vacuolation or vesiculation. If the epithelium becomes too loaded with transudate, sections of cells will be sloughed so that areas of connective tissue will be bared. As the disease progresses the edema of the conjunctiva seems to subside.

Round cells, usually plasma cells, appear in the connective tissue layer and seem to

migrate toward the epithelium. Scattered eosinophils may appear in the deeper layers of the connective tissue. The cells of the epithelium become increasingly more flat; the nuclei disintegrate and disappear. Finally the epithelium takes on a hyaloid appearance without definite cell walls and with scanty nuclei. On those portions of the globe where the epithelium of the bulbar conjunctiva is particularly flat, goblet cells will be absent.

Sjøgren[12] has pointed out that these changes in the bulbar conjunctiva are similar, histologically, to the changes which occur in the conjunctiva after extirpation of the lacrimal gland.

In the cornea, the epithelium will show areas where the protoplasm has become fibrillated in appearance and the cell layers have become thinned and attenuated, with subsequent sloughing of the superficial cells. This gives the surface of the cornea an uneven appearance and castoff superficial cells are responsible for the stippled effect seen with the aid of topical dyes.

In other areas, all layers of epithelium seem to be undergoing decomposition so that they appear as foci of degeneration. Similar appearing and sharply defined foci of degeneration may also occur in the corneal parenchyma.

Treatment

The treatment of this annoying ocular condition has been directed essentially along two basic lines. In one approach, therapy has been directed toward what was believed to be the probable cause of the disease. In the other approach, therapeutic measures have been proposed to alleviate the ocular symptoms. Since the cause of the disease is by no means definitely settled, treatment directed toward this facet of the disease leaves much to be desired. In some respects the forms of treatment directed toward the alleviation of the ocular symptoms have been more successful.

As regards the cause, four main hypotheses have been developed during the evolution of thought concerning the disease. These may be summarized as a belief that the disease is due to some chronic infection or toxin, that it is related to avitaminosis, that an endocrine factor is responsible, and that a trophic change has occurred because of some disturbance in the autonomic nervous system.

Sjøgren[2, 3] in his earlier publications championed the belief that a chronic infection is responsible for the condition, because of the elevated sedimentation rate, the lymphocytosis, secondary anemia, and polyarthritis that were quite frequently noted. Subsequent writers have referred to obscure toxic elements superimposed on infections. Beyond "measures to improve the general health" of the patient no specific measures have been proposed to combat this alleged cause.

The possibility that the disease is related to some disturbance of vitamin metabolism has provoked considerable comment in the literature. Successful treatment with large doses of vitamin A (Stahel,[82] Mørch[62]), with vitamin-B complex (Franceschetti,[37] Riva,[68] Iversen[60]), and vitamin C (Hansen[42]) has been recorded. I have treated a few patients with large doses (150,000 units daily) of vitamin A over periods of several months without observing definite improvement.

Fried and Goldzieher[38] treated one patient with vitamin A, and Lutman and Favata[46] utilized both vitamins A and B in one case without improvement. One of the stumbling blocks in accepting this hypothesis of avitaminosis and evaluating the therapeutic value of vitamin A has been an inability to demonstrate an avitaminosis A by biophotometric measurements. Godtfredsen,[39] although pointing out certain clinical features common to ariboflavinosis and Sjøgren's syndrome, was unable to improve the condition of his patients with vitamin-B and iron therapy.

Because of the age and sex incidence of the patients reported in the literature, the

belief that an endocrine dysfunction is responsible for the disease has become widespread. Most attention has been directed to the ovaries, but records of the treatment carried out for the supposed abnormality are very sparse, perhaps because the endocrine therapy has been unsuccessful. Fried and Goldzieher,[38] however, expressed the opinion that the therapeutic measures along these lines have not been sufficiently inclusive or extensive, for they reported remarkable improvement, "practically amounting to a cure," of a patient treated with estrogens over a three-year period. The reader is referred to their publication for the details of this successful treatment.

The occasional encounter with a patient who complains of an inability to sweat along with the ocular disability has stimulated therapeutic measures directed toward the autonomic nervous system. Physostigmine has been used without success by Beetham[20] in the treatment of one patient. Gifford, Puntenney, and Bellows[22] employed prostigmine in the treatment of five patients with some benefit, but they did not have an opportunity to observe the efforts of this treatment over a long trial period. I have not found definite evidence of improvement among the few patients whom I have treated with prostigmine.

One of the most remarkable of the successful treatments that have been reported is contained in the publication by Leriche.[44] Because of the lack of tears, dry mouth, and changes in the skin of the face that he had observed in one case, he reasoned that some disturbance in the circulation of blood to the face had occurred. To combat this deficiency in the facial circulation he carried out a bilateral section of the vertebral nerves and a bilateral resection of a portion of the superstellate segment of the cervical chain including the intermediate ganglion. Within a period of about six months the moisture in the mouth had returned and the patient was able to shed "a few real tears." The patient was followed for a period of 28 months and finally succumbed to a "hemorrhagic purpura."

On the basis of some beneficial results reported by Schall,[75] "minimal stimulating" doses of roentgen rays to the lacrimal gland have been tried by Fried and Goldzieher,[38] and by Beetham.[20] They were unsuccessful in duplicating the improvements that Schall[75] had reported. Schall treated patients who had filamentary keratitis but, because in so many of the 10 cases that he reported the lesions were unilateral, there is some doubt as to whether they were true cases of keratoconjunctivitis sicca.

As regards the measures proposed for the relief of the ocular symptoms, some type of eye wash or solution may be employed, or the lacrimal puncta and canaliculi may be closed as in the method proposed by Beetham.[20] Various collyria have been used in an attempt to alleviate the annoying symptoms caused by the erosions on the surface of the cornea and the accumulation of mucus in the fornices. A mild antiseptic might be indicated during the episodes of redness to combat the secondary infection.

Collyria, such as the ones proposed by Rucker,[49,50] have been prepared to resemble tears. My colleagues and I have used both his one-percent gelatin in Locke's solution and 10-percent blood serum in Locke's solution with symptomatic relief in some instances.

More recently commercial preparations of methyl cellulose have appeared on the market as "artificial tears." All of these preparations are designed to keep the cornea moist, and no one preparation seems to benefit all patients. A satisfactory collyrium to bring relief from the symptom of burning has not been found. Oftentimes plain water turns out to be the best all-round eye wash from the patient's standpoint.

Since Beetham[20] first proposed the electrocoagulation of the lacrimal puncta and canaliculi, this method of treatment has been widely employed to bring symptomatic relief to the patient. Beetham reasoned that,

if all tear drainage channels were closed, the diminished supply of tears in the conjunctival sac would be better utilized. Beetham in his original description of the method reported on the relief obtained in eight eyes as "immediate and remarkable."

Bruce[31] spoke of "instantaneous and permanent" relief in the cases in which this method of treatment was used. De Roetth[34] referred to "immediate and dramatic" results and expressed the opinion that fulguration of the puncta and canaliculi is the best procedure for the treatment of keratoconjunctivitis sicca. Gifford, Puntenney, and Bellows[32] seemed favorably impressed with the results obtained in their cases and stated that decided improvement of vision can be expected in those cases wherein the vision is blurred as the result of numerous corneal filaments and erosions. Godtfredsen[39] expressed the belief that this treatment generally improves the patient's ophthalmic symptoms.

Rucker,[49,50] in his cases, found that fulguration did not always bring complete relief and supplemented the postoperative treatment with one of his solutions resembling tears. Lutman and Favata,[46] and Fried and Goldzieher[38] each reported one case in which the condition of the patient was not improved by the closure of the puncta and canaliculi. In Fried and Goldzieher's case the improvement was only temporary.

Proponents of this method of treatment naturally would question in these unsuccessful cases whether drainage channels had remained sealed, for it is realized by most ophthalmologists that the puncta and canaliculi may reopen and nullify the effect of the fulguration. On the other hand it might be reasonably asked if this treatment gives lasting benefits in all cases.

To clarify this question I corresponded with the patients in our series of cases who had undergone a fulguration of the puncta and canaliculi as a treatment for keratoconjunctivitis sicca. I received replies from 30 patients. Because I had anticipated receiving rather favorable reports on this method of treatment I was surprised at some of the answers that were received. In some instances among these 30 cases, my colleagues and I were able to confirm the follow-up study by reëxamination of the eyes. In only 10 (33 percent) of the 30 cases was there evidence that the fulguration of the lacrimal puncta and canaliculi had brought relief from the ocular symptoms or had resulted in improvement of the eyes. The follow-up period in this series of 10 patients ranged from 1½ months to 72 months with an average of 27 months after the electrocoagulation operation.

In the remaining 20 cases (67 percent) either the patients felt that their symptoms were unchanged as the result of the treatment, or reëxamination of the eyes showed the ocular signs to be essentially the same as before electrocoagulation. A few in this latter group actually complained that their eyes had been made worse, since the tears would pool at the inner canthus and run over the cheek. The follow-up period on these 20 patients ranged from 1½ months to 96 months and the average interval after the electrocoagulation procedure was 25 months.

The data obtained from the 20 who had not felt improved by the procedure after variable intervals of time were of further interest in view of the fact that these patients had all expressed approval and enthusiasm for the treatment immediately and within a few days after the procedure had been performed. I, too, have noted in most cases a distinct improvement in the ocular condition and a dramatic amelioration of symptoms immediately after this procedure, and I was under the impression that the results would continue to be favorable after these patients left our care.

The factor responsible for the immediate but temporary improvement in these cases might be the reflex lacrimation that is induced by the manipulation of the eyelids and the trauma created by the fulguration proc-

ess. It is conceivable that the lacrimal gland, although partially atrophied, would retain its ability to secrete an extra quantity of tears under a suitable stimulus, and then revert to its hyponormal rate of secretion once the emergency had passed. Of course in some cases, the disease continued to progress after operation, so that there were practically no tears secreted and this would account for some of the findings and reports of "no improvement."

Among the dissatisfied patients who were annoyed by epiphora as the result of the operation, it is possible that the disease had undergone a temporary spontaneous remission so that a more normal flow of tears resulted and adequate drainage channels were unavailable. I have observed temporary remissions among patients who have had no other treatment except bland collyria.

From the data gathered in this series, then, it would seem that electrocoagulation of the puncta and canaliculi does not seem to produce the alleviation of the symptoms of this disease that one might at first assume.

Comment

With the impetus that Sjögren gave to the study of the syndrome that now bears his name, most ophthalmologists have acquired a reading knowledge of keratoconjunctivitis sicca in the sense that it comprises an integral part of this symptom complex. As a disease entity affecting the eye alone it seems less well known, for there are relatively few reports dealing with the ocular features of the disease and even fewer instances wherein a survey of a large series of cases has been undertaken. At first glance it would seem that the relative infrequency of the disease would make it difficult to assemble a large series of cases for study, but more likely the chief factor responsible for this state of affairs is that the disease is not recognized.

As pointed out earlier in this paper, the association of certain subjective symptoms does not occur frequently enough to constitute a distinctive feature of the disease. Furthermore, when certain symptoms that seem to be characteristic of the disease occur in the patient's story, the ophthalmologist may be unaware that keratoconjunctivitis sicca should be considered in the differential diagnosis. Too often these patients are treated for what seems to be a chronic conjunctivitis, or are given a new prescription for their refractive error because of symptoms resembling asthenopia. The chronic nature of their complaints may even catalogue these patients as suffering from psychoneurosis.

The problem of diagnosis, then, revolves around a measurement of the tear secretion, the instillation of a suitable dye into the conjunctival sac, and the examination of the cornea and conjunctiva with the slitlamp. These may be time-consuming procedures, particularly in a busy office practice but, until such examinations are routinely performed, the eye condition will continue to pass unnoticed and our knowledge of the disease will remain at a relatively stationary level.

Since the disease seems intimately associated with some alteration in the tear supply to the eye, it would seem logical to direct more attention in the future to this phase of the problem. Almost every observer who has utilized the test devised by Schirmer[20] for the quantitative measurement of lacrimation has either commented on or realized the limitations of this test. Owing to improper technique, the filter paper may be placed so that it will irritate the conjunctiva and even the cornea, thereby causing a reflex lacrimation and leading to a false result; or the paper may be insufficiently hinged on the margin of the lid and so give the impression that there are fewer tears than actually exist. Basically the filter paper test remains as a measurement of the tears present in the conjunctival sac at any given moment and, as some have pointed out, there should be a more reliable method for measuring the tears secreted direct from the

lacrimal glands. Until a more reliable and quicker method than Schirmer's is devised we must be content to employ this procedure only as an aid to diagnosis.

What constitutes a deficiency in the quantity of tears remains a matter of general disagreement. There have been surprisingly few data published on the normal tear secretion among persons of different sexes and various age groups, and until these factors are more definitely established one cannot say dogmatically that 10 or 15 mm. in five minutes of wetting of the filter paper strip constitutes the lower limit of normal.

Furthermore, it is now known that some persons seem to show a deficiency in the quantity of tears as measured by the Schirmer method but do not exhibit any defects in the surface of the cornea or conjunctiva. This might imply that the measurement of tear secretion is entirely unreliable as a diagnostic aid.

Vice versa, I have observed patients who present symptoms of the disease and show erosions of the cornea but who possess almost a normal tear supply. These phenomena may be due to an alteration in the quality of the tears rather than a deficiency in the quantity, a possibility that has not been considered heretofore. To date I am not aware of any research on the chemistry of the tears among cases of keratoconjunctivitis sicca.

Alterations in the surface layers of the cornea are the most reliable from the standpoint of diagnosis. They also serve as an index to the severity of the disease. The stippling effect as brought out by the fluorescein dye probably represents the initial changes in the corneal epithelium. The appearance of the cornea in this phase of the disease is akin to the descriptions given for "recurrent erosions of the cornea." It seems possible that in many cases in which a diagnosis of "recurrent erosions of the cornea of unknown etiology" has been made the lesions are in reality mild forms of keratoconjunctivitis sicca. The small, usually circular shaped, staining foci that seem to involve the thickness of the corneal epithelium probably represent the next phase of the disease from the standpoint of severity.

In the most severe phase, the epithelium peels away in threads and filaments. It is this phase of the disease that has been included under the descriptions of filamentary keratitis. Since there are factors other than a deficiency of tears that may produce the picture of filamentary keratitis, the retention of this term in ophthalmologic nomenclature would seem justified. However, in my opinion filamentary keratitis is more often the result of a deficiency of tears than of any other cause and from this standpoint the term should be less often used in favor of the more descriptive term "keratoconjunctivitis sicca."

If it can be argued that the term "filamentary keratitis" is merely a descriptive term for one phase of a disease entity, so then is the term "keratoconjunctivitis sicca." "Keratoconjunctivitis sicca" is a more inclusive term than "filamentary keratitis," but it too, only describes the disease as it affects the cornea and conjunctiva.

As both de Roetth[33] and Gifford and associates[32] have pointed out, keratoconjunctivitis sicca probably represents only one phase of the disease characterized by hypofunction of the lacrimal gland. I agree with these observers that there are some persons who possess symptoms very suggestive of the disease, who exhibit a decreased lacrimation, but who do not show any changes in either the cornea or the conjunctiva. In some of these patients corneal and conjunctival changes eventually develop, making possible a diagnosis of keratoconjunctivitis sicca.

Gifford, Puntenney, and Bellows[32] devised a classification based on the assumption that the disease entity is due to a hypofunction of the lacrimal gland. In Group I they placed patients who exhibited a deficiency of tear output but who did not show any alterations in the conjunctiva or cornea. In

Group II were placed the patients who showed the changes of keratoconjunctivitis sicca as they have been described in this discussion. In Group III they placed the patients who showed not only keratoconjunctivitis sicca but some extraocular manifestation of the disease (Sjøgren's syndrome). Such a grouping has the commendable feature of emphasizing that keratoconjunctivitis sicca and also Sjøgren's syndrome are but single phases of an over-all disease entity.

Perhaps it would be best, for a better understanding of the disease, to discard the term "keratoconjunctivitis sicca" in favor of some term which includes all phases of the ocular condition. "Hypofunction of the lacrimal glands" seems to be a suitable term but it has not caught the general ophthalmologic fancy and it will not easily replace the term "keratoconjunctivitis sicca." Sjøgren[11] proposed the term "dacryosialoadenopathia atrophicans" but this term is not applicable to those cases in which extraocular manifestations are not present.

From the classification such as Gifford and associates[22] proposed, and from the remarks about keratoconjunctivitis made in this paper, one might assume that in all cases the disease tends to progress to a final conclusion once the lacrimal glands are affected. A tendency to progression is not always present, however. In fact I have observed some cases in which the lesions tend to progress to a certain degree of corneal change and then remain at this level of severity for many years without getting any worse and without receiving any specific treatment. In a very few instances a rather permanent improvement seems to occur.

Most of the cases are characterized by temporary remissions of some degree. I have not discovered any particular characteristic among any of these cases to enable me to predict the course of the disease. It is the cases in which the disease progresses downhill rather rapidly over a period of several months to several years in spite of any treatment that offer the greatest challenge and cause the most concern to the ophthalmologist.

As mentioned previously it has not been my misfortune to see any permanent damage occur to the cornea even in the severer cases. It is true that the visual acuity may be moderately reduced by the changes in the cornea and the patient may be severely inconvenienced by the ropy secretion and the sensations of burning and scratching; yet he can maintain a reasonable mode of living so long as the eyes are solicitously washed and moistened and secondary infection is promptly treated when it occurs.

At the present time, it seems certain that some cases of keratoconjunctivitis sicca are closely linked with disabilities affecting other mucous surfaces. The mucous surfaces of the mouth and upper part of the respiratory tract seem to be the ones chiefly affected by the same disease process that affects the eye. A decrease in salivary secretion also occurs when the salivary glands are affected. Pathologic examination has shown that similar degenerative changes affect the lacrimal glands as well as the salivary glands. It is interesting to speculate on the reason for this close association in some cases.

Not all cases of keratoconjunctivitis sicca will develop the symptom complex wherein the mouth and mucous membranes of the upper part of the respiratory tract also become dry. On the other hand not all cases of xerostomia will exhibit the ocular changes. Just what factors are necessary for the development of the Sjøgren complex is not clear. Sjøgren[1,3] once thought that chronic infection played the major role in the development of the symptom complex but he has since discarded this hypothesis.

From the series of cases that I have collected it is not possible to say that involvement of mucous surfaces other than the eye will logically follow the involvement of the eye, for in many cases xerostomia and lack of salivary secretion have constituted the initial phase in the development of the syndrome. It is not possible to predict the order

of development of the various phases of the syndrome.

Contrary to the opinion expressed by many observers who have reported cases of Sjøgren's syndrome, I do not feel that polyarthritis is an integral part of the symptom complex. It is my feeling that arthritis is rather an incidental finding. Curiously, there has been little investigation of this phase of the problem by rheumatologists. Stenstam,[33] it seems, has been the only rheumatologist who has investigated a large number of arthritic patients with the possibility of keratoconjunctivitis sicca and xerostomia in mind. He felt that it was improbable that arthritis was part of the Sjøgren syndrome or was characteristic of keratoconjunctivitis sicca.

The etiology of keratoconjunctivitis sicca either as it manifests itself in the eye alone or as part of a wider symptom complex remains a puzzle. That some change in the lacrimal glands occurs which affects the eyes through the medium of the tears now seems certain, but the initial factor which causes the lacrimal gland to undergo degeneration remains obscure.

Although there has been much speculation among the reports in the literature that some endocrine basis for the disease exists, there is little proof from the standpoint of therapeutic results to confirm this hypothesis. However, that an endocrine or hormonal basis for the disease exists remains an attractive possibility. Particularly is this so when it is recalled that the disease is predominantly found among women.

Chronic infection certainly does not seem to be a factor among the patients who exhibit the ocular manifestations alone. In those patients who present the symptom complex such an infection might conceivably play a role, particularly among those who seem to show other signs of debility and accelerated aging. The possibility that some inherent defect exists in the nutritional or vascular supply to the affected glands should be investigated further.

Finally, the problem of why the conjunctiva undergoes an edema and then a hydropic degeneration should receive further study since such changes are not those commonly observed with a true desiccation. It seems possible that there are factors other than a limitation of the quantity of tears which cause the changes in the cornea and conjunctiva.

Until these problems are answered or partially solved the treatment of the annoying and sometimes disabling eye condition must remain on a symptomatic basis. There seems to be no local treatment for the eye that helps all patients. Even the method of fulguration or electrocoagulation of the lacrimal puncta and canaliculi which has been so enthusiastically received seems to have its limitations when the patients are followed over a long period.

Keratoconjunctivitis sicca, then, seems to be but one phase of a disease which affects both eyes in approximately equal intensity and is caused by an altered function of the lacrimal glands of unknown etiology. Its distribution among both sexes and various age groups is probably more common than has heretofore been realized.

The Mayo Clinic.

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POLYSACCHARIDES IN OCULAR TISSUE*

ROBERT DAY, M.D.
Baltimore, Maryland

The animal polysaccharides are a poorly understood group of biologic compounds of importance in ocular physiology as well as in diversified general functions of the body. They may be classified as mucopolysaccharides, mucoids, or glycoproteins, all of which contain hexosamine. The mucopolysaccharides are free carbohydrates or so loosely attached to proteins that they are easily hydrolyzed; they may be simple, containing acetylated hexosamine; or complex, containing sulphates, phosphates, or lipids. In the mucoids and glycoproteins the polysaccharide fraction is firmly bound to the protein. The mucoids contain considerable hexosamine; whereas, the glycoproteins contain little.

The study of the animal polysaccharides is difficult since they are not only complex but are also often impossible to detach in unaltered form from other tissue components. In 1893, Morner[1] obtained from the vitreous humor of cattle a carbohydrate-protein complex responsible for its viscosity. In 1925, Levene[2] identified the polysaccharide moiety of this as containing glucuronic acid, acetylglucosamine, and sulfuric acid.

In 1934, Meyer and Palmer[3] isolated, again from cattle vitreous, a viscous carbohydrate of high molecular weight which did not contain sulfuric acid. He believed Levene's analysis to have been partially incorrect. Meyer called this polysaccharide hyaluronic acid. The isolation of hyaluronic acid soon led to its discovery in skin, synovial fluid, umbilical cord, unfertilized ovum, capsules of many bacteria, and tissues of many animal species.

Meyer,[4] in 1937, discovered in an autolysate of Type-II pneumococci an enzyme which depolymerized hyaluronic acid, destroying its viscosity. Similar enzymes were soon found in many other bacteria, in skin, in snake venom, and in extracts of various mammalian tissues, among them iris, ciliary body, and testis.

In 1939, two English workers, Chain and Duthie[5] identified hyaluronidase with certain spreading factors present in many bacteria which had been under study since 1928 and which were concerned with the extension of bacterial infection through the extracellular tissues. Thus, the principal organic constitutent of the vitreous, hyaluronic acid and the enzyme hydrolyzing it, were found to have widespread biologic importance.

Meyer[6] found that the aqueous contains both hyaluronidase and hyaluronic acid, the latter being in highly depolymerized form. He hypothesized that some cases of deep-angle glaucoma might be the result of an imbalance between the formation of hyaluronic acid presumably in the ciliary body, and its depolymerization, either by the aqueous or elsewhere. Meyer[7] also isolated a polysaccharide from the cornea which he thought to be a monosulfuric acid ester of hyaluronic acid. Since this was not present in the sclera, he thought the corneal transparency might be related to the presence of this substance.

Several histochemical techniques have been used to identify tissue polysaccharides. Until recently these have been empiric rather than rational. During the war, however, Hotchkiss[8] revived a technique, which had been applied 10 years earlier to cellulose and starch, that specifically oxidized 1.2 glycol groups to aldehydes which were then stained by Schiff's reagent. This technique was qualitative rather than quantitative and was most easily applied to those polysaccharides which were not easily dissolved during fixation. Friedenwald and Becker successfully applied this technique to the eye.

* From the Wilmer Ophthalmological Institute of The Johns Hopkins University and Hospital. Presented at the 18th scientific meeting of the Association for Research in Ophthalmology, Philadelphia, June, 1949.

Preliminary observations

The following preliminary observations were made in order to point the way to more precise and quantitative studies of the ocular distribution and biochemistry of these polysaccharides.

All basement membranes, such as Descemet's, Bruch's, and the lens capsule, stained intensely by the Hotchkiss-Friedenwald technique. Furthermore, a basement membrane was found to line the entire vascular tree as well as the entire subepithelial portion of the ciliary body. The corneal epithelium and the outer half of the rod and cone layer of the retina stained slightly less intensely. The internal limiting membrane of the retina stained deeply and in this property differed from the outer limiting membrane. The corneal stroma, the supporting structure of the optic nerve, and the ciliary muscle stained less strongly. The sclera, the inner half of the rod and cone layer, and the vitreous stained faintly. Other structures stained little or not at all.

Sections of cornea from cattle, rabbits, rats, and humans were incubated with salivary amylase for periods up to two hours after alcoholic fixation. The corneal epithelium contained a substance stainable by the Hotchkiss technique which disappeared after salivary digestion. This is presumably glycogen.

The same corneas were also incubated with bull testis hyaluronidase* which is known to accelerate the hydrolysis of the polysaccharide obtained from the corneal stroma. This crude enzyme caused not only the corneal epithelium but also the corneal stroma to lose its staining properties and apparently brought about the rapid depolymerization of both the stromal and the epithelial polysaccharide.

The ciliary body is thought by many to be the site of formation of hyaluronic acid. In several eyes clumps of deep-staining material were seen near the ciliary epithelium; in some eyes these clumps were in loculated pockets completely surrounded by ciliary structures. If these deposits were hydrolyzed by hyaluronidase, further presumptive evidence could then be adduced to support the ciliary theory of the formation of the vitreous.

In some of the eyes studied the enzyme apparently reduced the amount of the ciliary polysaccharide without visibly affecting other polysaccharide-containing structures of the same eyes. Proteolytic effects of the enzyme were also observed. Obviously accurate conclusions cannot be drawn from the use of so crude an enzyme mixture upon a substrate of unknown structure.

In ocular disease several substances have been observed to stain by the Hotchkiss technique; transudates, exudates, the colloid excrescences of Bruch's membrane known as Drusen bodies, and the hyaline tissue of many degenerative processes. Some melanomas contain a stainable material which disappears after salivary digestion. In the nerve-fiber layer of degenerated retinas intensely staining globules often can be seen which are not present in normal retinas.

Aneurysms of diabetes

A particular use of the Hotchkiss technique has been in the study of the capillary aneurysms of diabetes, recently described by Dr. Friedenwald in the Jackson Lecture.[9] These aneurysms are minute saccular dilatations of the capillary wall, apparently of the basement membrane of the capillary, and are usually near the arterial end of the capillary. They frequently have a laminated appearance, whether from reduplication of the membrane or because of hyalinization of successive layers of exudate it is difficult to say. At any rate there is a disturbance of the polysaccharide-containing portion of the capillary, unlike that of other diseases of the retinal vessels.

The clinical impression that these aneurysms are characteristic of chronic diabetes is not entirely born out by the study of autopsy material. A few isolated aneurysms are

* Supplied by the Schering Corporation.

occasionally to be found in chronic hypertension in the absence of clinical diabetes. Becker and Post[10] have found aneurysms near the venous end of the capillaries in several cases of occluded central retinal vein. In the latter instance, they are associated with generalized capillary dilatation, and with marked hemorrhagic and exudative retinitis and appear to be directly related to the increased pressure within the retinal veins.

We were particularly interested in the glomerular lesion of the Kimmelstiel-Wilson syndrome which also is found only in chronic diabetes. The possibility exists that the hyaline glomerular masses characteristic of intercapillary glomerulosclerosis, if not themselves aneurysms, are secondary to aneurysmal dilatations of the glomerular capillaries. Because of the anatomic peculiarities of the glomerular tuft it has, so far, been impossible to prove that the retinal and renal lesions are identical. There is good presumptive histologic evidence, however, that they are.

Thick sections were made of the brains in several cases of combined diabetic retinitis and intercapillary glomerulosclerosis. Only 1 or 2 lesions were seen which resembled the capillary aneurysms of the retina.

A few lesions resembling capillary aneurysms were seen in the capillaries of the fingernail folds of a number of living patients with diabetic retinitis.

From the information so far available, it is apparent that the capillaries of the retina are selectively though not exclusively involved in the aneurysm-producing phase of diabetes. The mechanism of the aneurysmal disease and of its relative selectivity for the retina is unknown beyond the fact that the normal polysaccharide pattern of the capillary bed is disturbed.

The Johns Hopkins Hospital (5).

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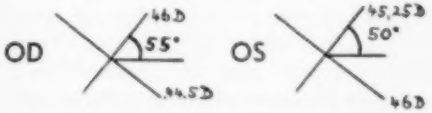
MEGALOPAPILLA: A NEW CONGENITAL ANOMALY*

A. Franceschetti, M.D., and R. H. Bock, M.D.
Geneva, Switzerland

The patient in whom this rare anomaly occurred was a young man, aged 25 years, who came to the clinic complaining of blurring of vision in the right eye for several years.

Examination showed vision to be: O.D., 0.7, with a 1.25D. sph. ⌒ −1.5D. cyl. ax. 145° = J1; O.S., 1.0 with a 1.25D. sph. ⌒ −0.5D. cyl. ax. 50° = J1.

Findings on the Javal ophthalmometer were:



Skiascopy showed the same findings as manifest refraction. Exophthalmometer readings (Hertel) were 19 mm., O.U.

The anterior segment appeared to be normal in both eyes. The corneal diameter was 10 mm. in each eye. Lens and vitreous were clear.

When the fundus of the right eye was examined through the undilated pupil, the visible field was at first found to be completely occupied by the disc which was of such size that its border was observed only after the pupil had dilated somewhat. The disc of the left eye also appeared to be enlarged, although not so much as the right (fig. 1). Except for this general enlargement, the discs were found to be completely normal; the outlines of the margins were sharp; the color was an even pink up to the border; no pigment whatsoever was present. There was no evidence of an excavation or of a conus.

After homatropine dilatation, the remainder of the fundus of both eyes was also found to be normal. The retinal vessels appeared somewhat narrow in relation to the size of the disc, although they were of absolutely normal caliber. The distance of the central macular reflex from the temporal border of the disc was about 1.5 prism diopters in the right eye and about 2.0 p.d. in the left eye (normal—about 2.5 p.d.). The unusual size of the disc explains this discrepancy.

An X-ray film (Rhese's inclination) showed the foramen to be somewhat large on both sides but still within the upper limits of normal. It measured 5 mm. on the right and 5.5 mm. on the left (upper limit—6 mm., Thiel).

The blindspot taken on the campimeter was enlarged in the right eye but normal in the left. The visual fields were normal for white and slightly constricted for red. The color vision, tested on Nagel's anomaloscope, showed a normal Rayleigh equation for both eyes.

General examination showed a strong, healthy individual of the pyknic-athletic type. His height of 170 cm. was the same as the length of the extended arms. The length of his hands and feet was normal in relation to the length of his extremities. Heart, lungs, and abdominal organs were without abnormalities. Sugar was present in the urine. His neurologic status was entirely normal.

As many members of the patient's family as possible were examined. His father had a somewhat enlarged disc of the left eye—although it was within normal limits; while that of the right eye appeared to be normal. Corneal opacities and a retinitis proliferans hindered the examination of his mother's fundi.

Two brothers of the patient—one of them a dizygotic twin—had discs of normal size. One sister could not be examined. The patient was not married and had no children.

* From the ophthalmological clinic of the University of Geneva. Director, Prof. A. Franceschetti. A short outline of this article was presented at the Reunion des Oto-Neuro-Ophthalmologues de la Suisse Romande in Neuchatel, October 31, 1948.

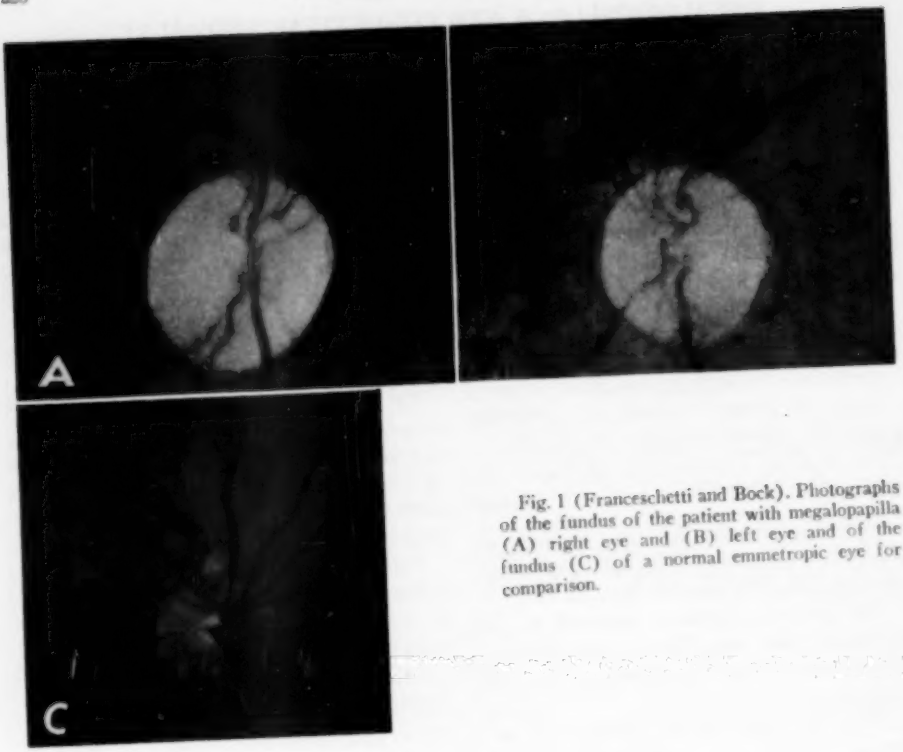
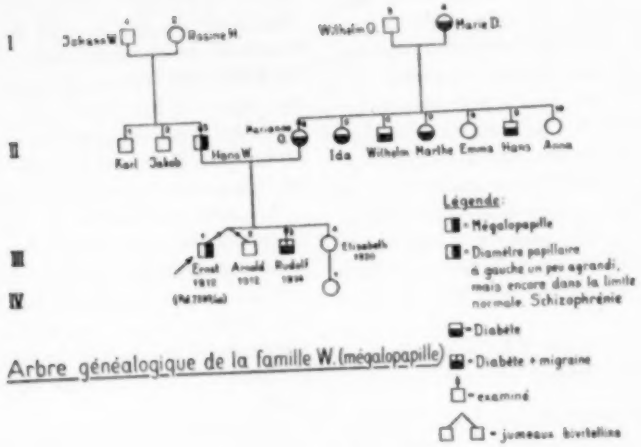


Fig. 1 (Franceschetti and Bock). Photographs of the fundus of the patient with megalopapilla (A) right eye and (B) left eye and of the fundus (C) of a normal emmetropic eye for comparison.



Arbre généalogique de la famille W. (mégalopapille)

Fig. 2 (Franceschetti and Bock.) Genealogic tree of the family of the patient with megalopapilla.

There was a diabetes with dominant heredity in the family (fig. 2).

Before any comment could be made on this interesting anomaly, which to our knowledge had not previously been described, it had to be proved that the disc was actually enlarged and that this enlargement was statistically significant. To clear this point, it was necessary to make direct measurements of the size of the discs in our patients and in a number of normal individuals as well. To accomplish this several methods were at our disposal:

1. Use of the direct ophthalmoscope which projects a graticule on the fundus (Morgan, 1927; Lambert, 1932, 1934). This would give inaccurate and only relative readings, however, for two reasons: (a) If either the patient or the observer has emmetropia, the correcting lens influences the magnification only if it is held exactly at the anterior focal distance of the eye, which is practically impossible; (b) the apparent magnification is arbitrary because it depends on the distance (usually taken as 220 mm. behind the eye) at which we project the image of the retina. Since this method of measurement is very simple, it is useful in emmetropic eyes and, when only approximate, relative values are needed.

2. More accurate results can be obtained by using an indirect ophthalmoscope of the Gullstrand type with a scale in the ocular or on the frontal lens (Spinelli, 1934; Bretagne, 1926; Dufour, 1926; Lobeck, 1934, 1941). From such readings, rather accurate absolute values may be calculated if the focal point of the frontal lens coincides exactly with the anterior focus of the eye. If this is not the case, a refractive error of the eye will influence the size of the image (fig. 3).

3. Another method would be to compare the diameter of the disc with the cross section of all the vessels at the disc border in photographs of the fundus. Measurements taken on photographs of normal fundi showed rather large variations with an average of 0.6:1 (total cross section of vessels in prism diopters). This comparative method was not accurate because both the disc diameter and the amount of blood in the retinal vessels vary greatly. Measurement of their thickness is also quite difficult on the usually somewhat blurred photographs.

4. For our examinations we used focal illumination of the fundus with the slitlamp (Haag Streit) and a contact glass (Goldmann, 1938) and made the observations through a microscope fitted with a micrometer scale in the eyepiece. This method gives accurate readings from which theoretically absolute values can be calculated.

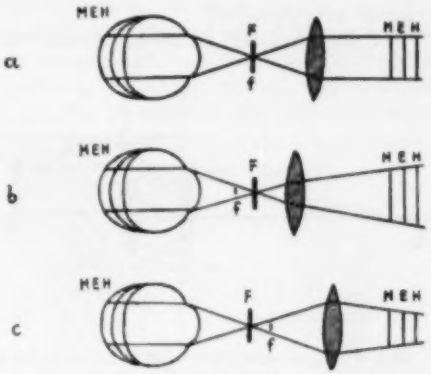


Fig. 3 (Franceschetti and Bock). The magnification of the image in indirect ophthalmoscopy (Duke-Elder, *Textbook of Ophthalmology*, volume 1, page 794): F = anterior focus of the eye. f = principal focus of the frontal lens. When the lens is at its own focal distance from the anterior focus of the eye (a), the magnification is the same in all refractive conditions; if the lens is less than its own focal distance from the anterior focus of the eye (b), the magnification is greater in hypermetropia (H) and less in myopia (M) than in emmetropia (E); and if the lens is further from the eye than this (c), the magnification is greater in myopia and less in hypermetropia than in emmetropia.

Technique employed

After instillation of 2 to 3 drops of larocaine (5 percent), the application of the contact glass is easy in a coöperative patient.

Homatropine cycloplegia is employed. In order to obtain accurate readings, it is important that a good target be used during the examination so that the patient can fix upon it easily.

Readings are taken as soon as both the beam of light and the microscope are focussed on the retina. Only an exact focusing will give correct readings. The possibility of errors (as demonstrated in Figure 3) is thus automatically excluded. Therein lies the advantage of this method.

For the calculation of absolute values, the following procedure is necessary: (1) Standardize the micrometer scale in the eyepiece—that is, calculate the magnification of the microscope used. To do this, focus on a very accurate stage micrometer and take the reading on the scale in the eyepiece. In our microscope there were: 45 subdivisions of the ocular scale equal to 4 mm., thus one subdivision was equal to 0.0889 mm.

In fundus observations, however, the magnification just described will vary, and this variation will change the refractive error of the examined eye.

We are dealing here with a refraction by a homocentric system of lenses. The easiest method to treat such a system is to take the image formed by the first refracting element (the lens) as object, the rays from which are to be refracted by the second element (the contact glass). See Figure 4. The calculation can be performed by two different methods which will serve as a mutual check for the final results.

First method

Excepting the lens, all the media behind the contact glass are considered as having a uniform refractive index of 1.336. The refractive power of the cornea can then be disregarded since its refractive index (1.376) is only insignificantly higher than the surrounding media on both sides.

Then the focal distances of the two lenses and of their optical centers are calculated.

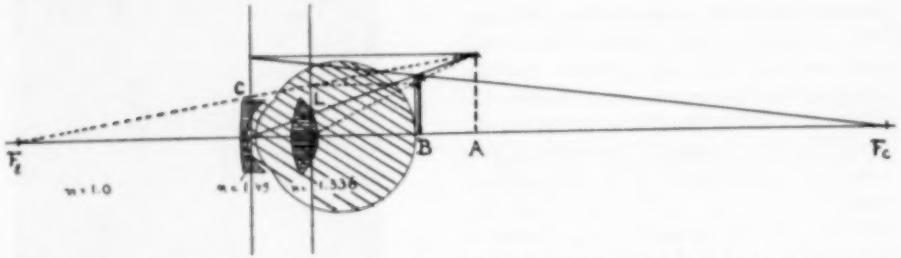


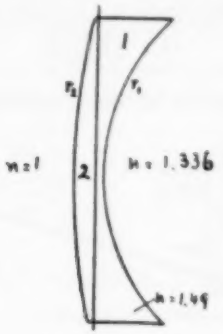
Fig. 4 (Franceschetti and Bock). Showing the homocentric system of contact glass (C) and crystalline lens (L). F_c = focus of the contact glass; F_l = focus of the crystalline lens. The image (A) produced by the lens (L) is at the same time object for the contact glass lens (C). B is the image of the combined system.

a. The contact-glass system. The contact glass which we used (Goldmann's, manufactured by Haag & Streit, Bern) is made of plexiglass with a refractive index of 1.49. It is convex-concave, with a radius of curvature of $r_1 = 8$ mm., $r_2 = 70$ mm., and has a thickness of 1.3 mm. at the center.

For the calculation of the focus, the contact glass has to be divided into a (1) plane-concave and (2) a plane-convex lens so that the different refractive indexes of the media in front and behind it can be taken into account.

For practical purposes, the refractive indexes of the media behind the contact lens (normal saline solution, cornea, aqueous, vitreous) can be taken as uniform with $n = 1.336$.

The imaginary plane surface is without influence on the refraction if the rays pass more or less parallel to the axis, and the foci for the two lenses (surrounded by a medium of n = 1 and n = 1.336, respectively) can, therefore, be calculated separately.



(1) Calculation of the focus f_1 of the plane-concave part of the lens:

$$\frac{1}{f_1} = \frac{n-1}{r_1} = \frac{0.115}{8} \text{ mm.}$$

$$\left(n = \frac{1.49}{1.336} = 1.115\right)$$

(2) Calculation of the focus f_2 of the plane-convex part of the lens:

$$\frac{1}{f_2} = \frac{n-1}{r_2} = \frac{0.49}{70} \text{ mm.}$$

$$\left(n = \frac{1.49}{1} = 1.49\right)$$

The focal distance of the contact glass is then:

$$\frac{1}{F} = \frac{1}{f_1} - \frac{1}{f_2} = \frac{0.115}{8} - \frac{0.49}{70} = \frac{4.13}{560};$$

F = 135.14 mm.

b. The crystalline lens. In this system, we can take Gullstrand's standard figures for the calculation. It should be kept in mind, however, that these figures may vary to a certain extent in normal eyes. Refractive power: 19.1D.; focal distance: 69.908 mm.

c. The distance between the optical centers of the two lenses. The optical center of the contact glass can be calculated as 0.167 mm. behind its concave surface. The distance of the anterior surface of the contact glass from the anterior surface of the cornea varies from 2.2 to 2.4 mm. and was taken as 2.3 mm. in this calculation.

Since the thickness of the contact glass is 1.3 mm., its optical center in position will be 0.83 mm. in front of the cornea and 7.91 mm. in front of the optical center of the lens. (In this calculation, we do not take the principal point of the total eye—1.35 mm. behind the cornea—but the optical center of the lens which is 7.08 mm. behind the cornea.)

d. The distance of the object (retina) from the optical center of the lens for different refractive errors was taken as:

Error	Distance
−9.0D.	20.56 mm.
−6.0D	19.39 mm.
−3.0D.	18.22 mm.
Emmetropia	17.05 mm.
+3.0D.	15.88 mm.
+6.0D	14.71 mm.

(3.0D = 1.17 mm.)

By using these data, the magnification can be easily calculated. It will be found that the magnifying effect of the lens will be almost compensated for by the contact glass. The final magnification calculated for a few refractive errors is shown in Table 1. It can be seen that, in order to obtain the actual size of an object observed at the fundus, it is necessary to multiply the readings on the ocular scale by the figure for magnification, as shown in Table 1, and the magnification of the microscope.

TABLE 1

MAGNIFICATION OF THE FUNDUS USING A CONTACT GLASS OF GOLDMANN

Refraction	Magnification
− 9.0D.	1:1.112 = 0.896
− 6.0D.	1:1.104 = 0.908
− 3.0D.	1:1.09 = 0.917
0.0D.	1:1.08 = 0.926
+ 3.0D.	1:1.07 = 0.935
+ 6.0D.	1:1.06 = 0.945
+10.0D.	1:1.05 = 0.955

SECOND METHOD*

Here we are concerned with the refractive powers of the two lens systems: (1) The contact glass plus the lens of saline solution between the cornea and the contact glass, and (2) the whole eye.

If we know the refractive powers of these two systems and the distance of their principal points, we can calculate the magnification.

2. The refractive power of the whole eye is (Gullstrand):

$$D_o = 58.64$$

Its principal point is 1.35 mm. behind the cornea; the distance between the two principal points is then

$$\delta = 2.18 \text{ mm.}$$

Gullstrand's formula for these two systems can now be applied:

$$B = A + D$$

where

$$A = 1/a;\ B = 1/b;\ D = 1/f$$

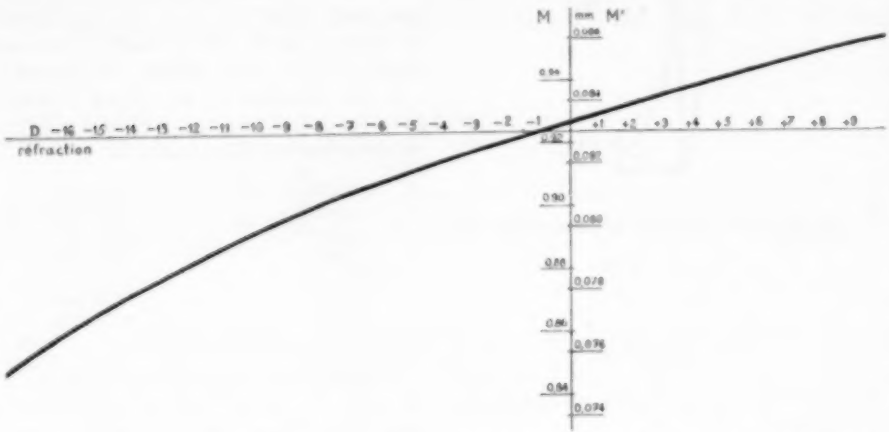


Fig. 5 (Franceschetti and Bock). Graph demonstrating the relation between the two variable M† (magnification of the fundus using a contact glass of Goldmann) and X (ametropia in diopters). M' is the actual size in mm. corresponding to one subdivision of the ocular scale in our slitlamp.

1. The contact glass-saline lens system:

$$D = 1/f = (n - 1) \cdot (1/r_1 - 1/r_2)$$

For the contact glass:

$n = 1.49$; $r_1 = 8$ mm.; $r_2 = 70$ mm. $D = -54.25$

For the saline lens:

$n = 1.33$; $r_1 = 7.7$ mm.; $r_2 = 8$ mm. $D = -0.16$

$D_{cs} = -54.41$

The saline lens is so thin that its optical center can be put together with that of the contact glass: 0.167 mm. behind its concave surface and 0.83 mm. in front of the cornea.

* Indicated to us by Prof. H. Hartinger of Munich.

† To obtain the actual size of an object observed in the fundus, the values of M have to be multiplied by the magnification of the slitlamp (in our instrument with 0.0889, see page 230, which will give us the figures indicated on the right side of the ordinate, M').

Let us take as an example a case with a skiaskopy finding of −3.0D. and a papillary diameter reading of 20 subdivisions on the ocular scale. The above curve now indicates that one subdivision of the ocular scale corresponds to 0.0824 mm. and this figure multiplied by 20 gives us 1.65 mm. as the actual size.

(a is the distance of the object; b is the distance of the image.)

First system

(contact glass + saline lens)

$$B_{es} = A_{es} + D_{es}$$

Second system

(ametropic Gullstrand eye)

$$B_e = A_e + D_e$$

(where) $A_e = X$ (ametropia in diopters)

The corresponding formula for the magnification is:

$$M_{es} = \frac{B_{es} - D_{es}}{B_{es}} \qquad M_e = \frac{A_e}{A_e + D_e}$$

$$b_{es} = \frac{1}{B_{es}} \qquad A_e = X;\ a_e = \frac{1}{X}$$

$b_{es} - \delta = a_e =$ (distance of image of one system minus δ = distance of object for the other system.)

$$\frac{1}{B_{es}} = \delta - \frac{1}{X}; \qquad B_{es} = \frac{X}{1 + \delta X};$$

$$M_{es} = \left(\frac{X}{1 + \delta X} - D_{es}\right)\frac{1 + \delta X}{X}$$

$$M_e = \frac{X}{X + D_e}$$

The final magnification M will be: $M = M_{es} \cdot M_e$

$$= \left(1 - \frac{1 + \delta X}{X} D_{es}\right)\frac{X}{X + D_e};$$

$$M = \frac{X - (1 + \delta X)\, D_{es}}{X + D_e}$$

This formula will give us the magnification for any degree of ametropia (X) and the values obtained are exactly the same as those found by the first method as shown in Table 1. (See also Figure 5.)

In all of these calculations, only the standard values of refraction of the normal eye have been considered. Any refractive error —determined by skiascopy—has been attributed to an axial ametropia. The rare possibility of an abnomal refraction of the media which is compensated by a change in the distance between nodal point and retina cannot be excluded if the length of the eyeball is not determined.

The length of the eyeball could be determined by the method of Goldmann and Hagen (1942) by means of X rays. However, the errors which are produced by such a refractive ametropia are probably very slight and are, therefore, unimportant in clinical observations.

In order to obtain an average of the size of the normal disc which would guide us in the interpretation of our case of megalopapilla, measurements were performed on 100 normal eyes.

Both the vertical and the horizontal disc diameters were measured. If the disc appeared to be oval in shape, and also if the two diameters were of absolutely different lengths, an average between the two was taken. After taking the refractive error into account, the actual size was calculated from

TABLE 2

DISTRIBUTION OF FINDINGS IN MEASUREMENTS PERFORMED ON 100 NORMAL EYES

Papillary diameter in mm.	0.1 mm. classes	1.20–1.29	1.30–1.39	1.40–1.49	1.50–1.59	1.60–1.69	1.70–1.79	1.80–1.89	1.90–1.99
	0.01 mm. classes	1.23 (1)	1.30 (1) 1.34 (1) 1.36 (2) 1.38 (1) 1.39 (1)	1.41 (2) 1.43 (3) 1.44 (1) 1.45 (2) 1.46 (1) 1.47 (1) 1.48 (4) 1.49 (3)	1.51 (6) 1.52 (2) 1.53 (1) 1.54 (2) 1.56 (2) 1.57 (1) 1.58 (3) 1.59 (2)	1.61 (4) 1.62 (3) 1.63 (2) 1.64 (3) 1.65 (1) 1.67 (4) 1.68 (3) 1.69 (2)	1.70 (2) 1.71 (3) 1.73 (3) 1.74 (2) 1.75 (5) 1.76 (2) 1.78 (3) 1.79 (2)	1.80 (3) 1.81 (1) 1.83 (1) 1.84 (2) 1.86 (2)	1.90 (1) 1.91 (1) 1.93 (1) 1.99 (1)
No. of observ.		1	6	17	19	22	22	9	4

$M = 1.6224 \pm 0.0153$
$\sigma = \pm 0.153$

$g_1 = -0.0950$
$g_2 = -0.4955$

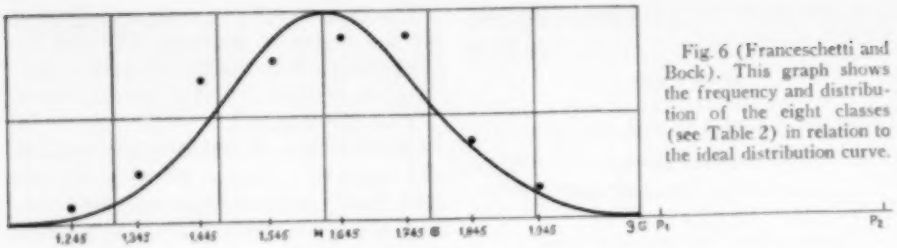


Fig. 6 (Franceschetti and Bock). This graph shows the frequency and distribution of the eight classes (see Table 2) in relation to the ideal distribution curve.

the measurements. The distribution of our findings is shown in Table 2.

The statistical interpretation of these values (taking 0.01 mm. as the size of each class) gave us a mean of

$$M = 1.6224 \pm 0.0153$$

and a standard deviation of

$$\sigma = \pm 0.153$$

Calculating the skewness ($g_1 = -0.0950$) and the excess ($g_2 = -0.4955$) of the sample we found no significant departure from normality. g_1 and g_2 are not significant compared with the sampling deviation of skewness ($\sigma g_1 = 0.2414$) and excess ($\sigma g_2 = 0.4784$) for a normal distribution (R. A. Fisher 1946).

The discs in our patient with megalopapilla were: O.D., 2.45 mm. and O.S., 2.11 mm., and were, therefore, significantly larger than an average disc, the deviation from the mean being greater than three times the standard deviation

$$M + 3\sigma = 2.0814 \text{ mm.}$$

It can also be easily shown graphically that our findings (taking 0.1 mm. as the size of each class) agree fairly well with the ideal curve of Gauss (see Feuzter, p. 264), as is illustrated in Figure 6.

Figure 6 also shows that the values for the size of the disc in our patient ($P_1 = 2.11$ mm.; $P_2 = 2.45$ mm.) are well beyond the normal distribution curve and 3σ.

Knowing that in a normal distribution we expect only 0.27 percent of the observations to lie outside of 3σ, and practically none outside of 4σ, we can say with certainty that we are dealing in our case of megalopapilla with a real anomaly.

Summary

A case of a patient with discs more than double the average size is described. All of the other findings were essentially normal. The foramina optica were large, and the corneal diameters were small, but both were still within normal limits.

For comparison, 100 normal discs were measured by means of focal illumination of the fundus with the slitlamp, using a contact glass of Goldmann and an ocular fitted with a micrometer scale.

For these readings, absolute values for the size of the various discs were calculated, taking into account the refractive errors.

Statistical interpretation of these findings proved that a real anomaly was present in the case herein reported.

3 Avenue de Miremont.

We wish to express our sincerest thanks to Prof. A. Linder and his assistant, A. Kaelin, for their interest and help with the statistical interpretations; and to Dr. D. Klein and Dr. P. Müller for their investigation of the patient's family.

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THE PSYCHOLOGY OF THE POOR READER*

WILLIAM H. CRISP, M.D.
Denver, Colorado

It seems well to confess that the subject dealt with in this paper is not strictly ophthalmologic, but rather pedagogic. On the other hand, the problem considered is one upon which the ophthalmologist will be frequently consulted, and to which his knowledge and skill may be usefully applied. Broadly considered, the problem has intimate association with the mysteries of the psychology of vision, as well as with educational method.

For some 6,000 years, written language, and the associated faculty of reading, have added enormously to the diffusion of knowledge. It is true that some great nations have existed in a general condition of illiteracy, while their people, through native arts and industries, developed a high order of intelligence. But the spread of knowledge of the world at large, the recording of the facts of the past, the fixation of laws and contracts, required the existence of an upper crust of population in which writing and reading were utilized. Russia is an especially great example of this truth, and the further expansion of Russia's intellectual development demanded the wider spread of literacy which Russia's government now proudly claims to exist in its citizens.

It seems obvious that spoken language must at first have been generally limited to words of one syllable, simple sounds which were later combined to deal with more complicated concepts. The earlier more or less hieroglyphic representation of language, and the use of complicated word signs, offered a much greater obstacle to the general spread and use of written language than the ultimate development of an alphabet in which each letter had a fairly definite and restricted value but with which an endless variety of new combinations were constantly available.

Until the present century the universally accepted way of approach to the acquisition of writing and reading skill had been first the teaching of the names and values of individual letters, then the construction of single syllables, and finally the progressive comprehension of words of several syllables. This, it is obvious, repeated rather closely the course of evolution of language.

Recent educational method, in various lines of so-called natural approach, has sought the avoidance of any element of the mechanical, so that, for example, the early singsong acquisition of the multiplication table, as a short cut to the elementary processes of

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arithmetic, has become taboo; and at the same time the routine learning of an alphabet and of spelling has been avoided and the youngster called upon to seize complete words and even phrases by the so-called "flash" method. We are confronted with a conflict between this flash method and the old phonetic approach. For the past few decades it has been rather generally considered heretical for a mother to teach her own child the alphabet and the rudiments of written speech before the youngster was taught in school. Fortunately a number of parents disregarded this modernistic educational dogma and so taught their children to read before the beginning of the first grade.

The types of reading difficulty with which we as ophthalmologists are most concerned do not seem to have a great deal of relation to the general mental capacity of the child. Some high-grade imbeciles read with great facility, although they fail to grasp the sense of what they are reading. On the other hand, many boys and girls are failures in reading although showing a high intelligence quotient.

The amount of refractive error has usually very little importance in relation to this problem, although we could make the mistake of failing to correct a refractive error which added to the patient's difficulties. We have no doubt all corrected low refractive errors without benefit to reading failures. Yet it would be foolish to ignore the possibility that the individual is baffled by a refractive error in his attempts to read.

Efforts have been made to argue that the poor reader has a definite brain defect analogous to that which sometimes occurs from injury, as urged by Hinshelwood,[1] one of the earliest inquirers into the problem. But there is no adequate evidence in this direction, and there are very substantial reasons to the contrary. Especially, it is difficult to explain upon the anatomic basis the very rapid progress made by many of the victims under intelligent remedial training.

A good deal has been said about a supposed connection of reading defects with left-handedness, particularly in regard to ill-conceived efforts to convert a left-handed child into right-handedness; and some cases definitely display more or less influence of this sort; but the general problem involves a much greater number of subjects in whom the handedness problem does not exist. The rare phenomenon of mirror writing has been found definitely associated with handedness, and yet now and then it appears to have an entirely different psychologic foundation.

Defects in reading ability range from extreme to moderate, and include especially confusion of one consonant with another, as b for d, p for q, t for f; reversal of the initial and final letters of words or syllables; misnaming of vowel sounds; insertion of sounds or words not included in the print or copy; and sometimes complete failure even to approach the recognition of a word. The partial reader may pick up many of the more usual words but may lose a great deal of time in the effort to make out less familiar expressions. Or he may lose time by hesitation and finish by completely misnaming the word. In any partial failures the difficulty may of course be more or less apparent according to the subject's degree of familiarity with the material presented, because the context may render possible a good many accurate guesses.

In the earlier school grades the fairly severe cases may show appreciable progress in arithmetic but a rapid falling behind in subjects where the reading ability is more essential. Some young children show surprising ability to repeat a whole page as read by a classmate, and yet are quite unable to recognize letters or short words when separated from the context. The more necessary progress in reading becomes for keeping up with the rest of the class, the more obvious is the child's retardation. He is then often credited with slow intelligence. A child of good general intelligence may go along to the high-school stage with passing grades, only to give more and more evidence he will not be

able to satisfy the requirements for entering college. His capacity for oral reading may be superior to that for silent reading, or vice versa. Recognition of his difficulty may be delayed by a retentive memory for what he hears in the classroom.

Commonly, even in the presence of an excellent intelligence quotient, the existence of merely a moderate reading difficulty may thwart eager ambitions and may distort the student's whole career. For one thing, such persons are likely to avoid general reading, or to have inadequate time for it, in spite of best intentions, and here again their general vocabulary is greatly limited and their ability to absorb further vocabulary along academic and scientific lines is constantly restricted or inhibited.

It may be possible to associate a few of the earlier cases with behavior complexes and the more obvious defects of home surroundings, but on the other hand the reading difficulty itself is capable of producing many complications as to the behavior of the individual, and there are numerous instances in which behavior improves in various ways under the influence of remedial training in reading. Often, however, it is impossible to identify any psychologic basis of the defect.

One writer reports that a number of his special problems were in children of former school teachers. Since the psychologic environment of the child begins at least at the cradle if not earlier, and the impressions, shocks, and conflicting influences go on usually for 5 or 6 years before the reading age, there are infinite possibilities for the creation of inhibitions or misdirections during these preliminary years as well as at the more or less sudden entry into school life. Broadly speaking, one element or another, sometimes several elements, in this tangle of psychologic influences must be held responsible for the tragic interference with satisfactory acquirement of the reading skill.

The faculty of speech, it must be remembered, is now generally regarded as having developed through a vast period of time, and very gradual must have been the supplemental process by which reading and writing were added to the power of speech. The necessity for training in this supplemental skill is presented to the child as a fairly abrupt transition.

The development of individual faculties must often depend upon the successful opening of new doors in the child's understanding and effort, and failure of these individual doors to open will often be due, not so much to congenital incapacity as to absence of favoring environmental influences in the child's psychologic experience, or to the existence of inhibiting or obstructing factors. Fear, anxiety, jealousy, rivalry, rebelliousness, inferiority complexes, a sense of loneliness in effort, may play important parts. Once the sense of difficulty or obstacle has been created, its mere presence has great power to interfere with progress, and the door that failed to open may remain closed. Among the hindrances, we must not forget excessive eagerness in a parent or positive dislike for a teacher, or the contagious personal reactions of schoolmates.

In the Institute for Juvenile Research at the University of Chicago there is a very striking preponderance of boys over girls in the cases of reading difficulty presented for attention. Monroe,[2] whose work was conducted in that institution, suggests that there may be an analogy between this fact and the relative incidence of color blindness in males and females. Such an explanation seems unlikely. We must not forget that there is often a distinct and early difference between the interests of the young of the two sexes, and also a variation as to the relative influence of maternal association upon boys and girls. Cases of reading difficulty could be expected under any method of teaching—yet some of them are certainly due to poor educational method.

Many reform movements in human relations have an excessive tendency to assume that the new is necessarily better than the old, not merely in some limited aspects, but

in every aspect. This is true of some educational reform movements. There is also a disposition to believe that new methods are superior to the old regardless of the size of the group to be taught or of the training and skill of the teacher.

Eminent among educational reformers was John Dewey,[3] who about 50 years ago vigorously promulgated the thought that too much importance had been attached to reading as a study to be pursued for its own sake. Because reading is not reality, the Dewey school decried the central importance of reading in life. Luckily there are still some educators who frankly consider learning to read to be the central objective of the first three grades in school. In view of the loss progressively sustained by those who in the first three grades have not acquired the art of reading and the ability to advance continuously in that art, I do not believe that the latter group of educators is far wrong.

Strang,[4] who deals especially with the problem as encountered (sometimes too late) in high school and college, lays down the principle that "pupils entering the fourth grade of elementary school may be expected to have mastered certain basic reading skills, without which their further progress will be impossible," although at the same time this author insists that the pupils must have acquired the habit of using these basic skills as a means of getting the thought of the passage and not as ends in themselves.

Although the old singsong teaching of the multiplication table has gone by the board, I can remember very well that in my own mind this approach to certain arithmetic data continued for a long time to serve useful purposes. Parallel with this discarding of old arithmetic method is objection to, and even at times prohibition of, the time-honored mode of teaching the alphabet and spelling in which also, some of us will remember, there was a good deal of classroom singsong. It has frequently been told me by a child's mother that teacher said she must not teach her boy the letters of the alphabet.

One purpose of the "flash" method, in which the child is supposed to learn to recognize the word as a whole, is apparently the subsequent acquisition of greater speed and facility in the act of silent reading. I am sorry to confess that I have not observed any greater speed or accuracy in the work of those subjected to the new method than among those who suffered under the old technique. Furthermore, it has seemed to me that definite psychologic advantage might be attached to the fixation upon detail associated with the older method. I believe there is also psychologic advantage in the association between mother and child involved in the preliminary home teaching which used to be, and perhaps still is, fairly common.

It is interesting to discover, among those who have made a special study of reading difficulties, and of remedial training to overcome such difficulties, a more or less frank acknowledgment that these difficulties are more frequent among pupils who have been taught by the "flash" method than among those who from the beginning have been subjected to the phonetic method, in which the alphabet and the construction of syllables are the basis of learning to read. It is also quite instructive to find these authorities stating that the progress of remedial training is much greater by resort to the phonetic method, intelligently applied, than if the "flash" method is persisted in.

As regards the incidence of the reading problem, Orton,[5] physician and neurologist, who made a lengthy study at the University of Iowa, declares frankly that children who had been taught by the "flash" method showed proportionally three times as many cases of reading difficulty as did those who had been taught by the phonetic method. Monroe,[2] at the University of Chicago, here and there seems almost apologetic in advocacy of the phonetic instead of the "flash" method for remedial purposes, but diplomatically straddles the educational fence as

follows: "The problem of educational instruction in reading is to find the methods which are best adapted to develop skill in reading in the majority of children. The problem of remedial instruction in reading is to find a possible method of learning for those children who have never been able to learn to read by methods adapted to the group." A little later Monroe says: "Although some methods which we have used simulate at first a mechanical approach to reading, we have not discarded them on that basis if they brought measurable improvement in reading without sacrificing comprehension." And again: "Although it is desirable to be a speedy reader, it is better to be a slow reader than a nonreader; . . . although it is desirable to be able to recognize large thought units, it is better to read sentences word by word, or words sound by sound, than not to read them at all; . . . although it is desirable to obtain meaning without the awareness of mechanics, it is better to get the meaning by mechanical steps than not to get the meaning at all."

The claim was of course made that to be taught to read by the "flash" method was to *avoid* reading "word by word" or 'sound by sound"; that it was "to obtain meaning *without* awareness of mechanics." Some of the fastest readers that I have ever known were certainly taught by the phonetic route, and, in spite of all its mechanical procedures, I suspect that they have profited by early formation of habits of precision in detail. The truth of my impression appears to be supported by Monroe's own statement that "Reëxaminations of children taught by phonetic methods show that, after the initial start in reading is made, the children become more and more like normal readers. The secondary links . . . become less in evidence and tend to disappear. Speed of reading develops gradually without specific pressure. Words are grouped into phrases and larger thought units. . . . Thus, it appears that the child ultimately builds up an organization of responses which is very similar to the usual reading performance of unselected children."

An encouraging comment by those taking part in remedial training of children who cannot read is that, after development of the power to read, the general behavior of the individual often shows rapid and substantial improvement. The patient's general psychology, it appears, has benefited from relief of secret conflicts, inhibitions and humiliations.

Considered in its sociologic aspects, the unsuccessful reader may perhaps be regarded as the largest educational problem of our day. Monroe,[8] basing her conclusions upon a reading index established as normal, declares that 12 percent of the general population may be considered as having reading defects. Many of these cases are severe, a moderate percentage borderline in character, some of them unable to become adjusted without corrective instruction; others are capable of carrying on their work without special help.

Once the problem has become established in the individual, there is some prospect that the situation may be improved by instruction in small groups at the hands of sympathetic, intelligent, and well-trained teachers. But in many instances individual instruction is urgently necessary. There are, of course, a number of cases in which either as a community enterprise or as a private undertaking the attempt becomes uneconomic in the sense that the results cannot be regarded as compensating for the outlay in money and time.

Except in the earlier stages, and in relatively favorable cases, parents, even if suitably equipped as to personal and intellectual capacity and in the amount of leisure available, are often unequal to the task of remedial training. Unfortunately the average school teacher, even if she could spare the time, is also unsuited, or will at least require special training.

All this adds up to an enormous further expenditure in our school systems. The sub-

ject appears to be one for required courses in all institutions for teacher training, particularly as regards ability to diagnose early the existence of the reading problem in the individual pupil, and to initiate steps toward correction of the trouble.

It is a pleasure to recognize today in elementary schools, and in educational literature, some reaction toward adequate teaching of the reading skill. A recent work by Gray,[6] of the University of Chicago, under the title of *On Their Own in Reading*, presents an excellent course in pedagogic method as applied to this fundamentally important subject. He declares that the "elaborate and extensive remedial programs in the intermediate and upper grades have been finally recognized for what they usually were—evidence of failure to provide adequate developmental reading programs in the elementary grades." Gray criticizes as hasty and imperfect some of the reactions toward old mechanical methods, in that they do not give sufficient attention to the interest factor in teaching young children. He also points out that "Unfortunately, during the last 20 years teachers have had very little preparation for the teaching of word perception and especially of phonetic analysis."

One may perhaps be permitted to ask why a teaching method that appears so greatly to increase the incidence of reading failures should have been so long persisted in. To the average person it may seem not unreasonable to suppose that brief exposure of the pupil's eyes and brain to a new word or group of words, without analytical preparation, would favor the very sorts of confusion as to spelling which are encountered most frequently in the poor reader, namely: faulty vowels, confusion between more or less similar consonants, and reversal of the sequence of letters or words. The emphasis on speed rather than accuracy in the development of this new skill must surely increase the subconscious sense of defeat and conflict in the child's mind, to be followed by failure in further efforts.

It is a common experience to find children, even before entering school, eager for acquisition of the ability to read. But the children are subjected to the complications and inefficiencies of group, instead of individual, teaching. In spite of the fact that most mothers are not professionally trained for the task, is there not good ground to suppose that the sympathetic bond between mother and child, and the fact that the instruction and help afforded by the mother are individual in character, create as a rule more favorable conditions for the first steps toward reading and the comprehension of the forms of words?

Some workers in this educational problem lay stress upon the idea that not all children reach at the same age the degree of intellectual development at which the reading skill may be acquired. But I believe the eagerness of most small children to busy themselves with the drawing of letters and words speaks against the general importance of this argument. I have never hesitated to encourage mothers to teach their children the letters before the usual primary-school age, and I have never experienced any reaction which seemed to speak against this practice. I have even wondered whether it might be well, on account of the benefit to be derived from individual instruction, to form classes in which young mothers might learn how to instruct the preschool child in the elements of reading.

Orton[5] very properly argues that no child of average intelligence or better, with tangible evidence of a reading difficulty, should be allowed to continue into his second year in schooling without an analysis of his condition. Special measures should be instituted, if necessary, "before he suffers the emotional disorders and language deficits which are usually cumulative from this time on."

Emphasis by ophthalmologists upon the need for return to older and more mechanical methods is well supported in the discussion of Rychener's[7] interesting paper before the American Academy of Ophthalmology and

Otolaryngology last year. The author himself, after remarking that educators are beginning to change their minds about the efficacy of the modern type of reading instruction, and that many of them now believe it desirable to go back to the phonetic method, goes on to quote the statement of one third-grade teacher that his school's reading disability problems had markedly decreased since reverting to the old phonetic method of training in the first few grades.

Ability to read is one of the most important skills to be acquired in intellectual development. Once the opportunity for an easy approach to this skill has been lost, the psychologic hindrances thus created may be fatal to advanced progress. Instead of reading being a pastime, it becomes a dreaded task. In later years, professional ambitions are thwarted, undesirable emotional reactions are created, personality is distorted.

The ophthalmologist has many opportunities for giving advice in regard to this problem. He will do well to entertain the problem in his consciousness and in his personal reading. Brilliant remedial success is claimed by workers using somewhat different methods of approach. The most conspicuous basis of these successes is probably the fact that they were largely attained by individual attention to the child. It seems emphatically desirable to recognize the problem as early and as fully as possible in the life of the individual, and there is much to be said for reversion, in the early school grades, to methods and principles which were for a while too readily discarded as old-fashioned, mechanical, and unscientific.

The special department of medicine in which this society has played so important a part has not only the right but the duty to express itself with regard to the reading problem. In his able discussion of Rychener's paper before the Academy, Kronfeld called attention to a special study on this subject which, in 1941, was presented by Angus MacLean to the Washington postgraduate course. In that presentation MacLean suggested that children with special reading disability would gain if instead of the usual "look and see" method another teaching method could be made available to them. Kronfeld remarks that so far as he knows that recommendation has not been followed by any school board in the United States.

The following general conclusions seem justified:

1. Refractive errors play a relatively small part in the problem of the poor reader, although they should still be kept in mind as one basis for the early inhibitions of childhood.

2. Acquirement of the ability to read well is still the most important purpose of the first 2 or 3 years of school, and failure to acquire this basic skill at the proper time is a cause of limitation and failure in later lines of endeavor. It affects the whole life of the individual.

3. It is essential to recognize the existence of the reading problem within the first year or so of schooling, and to take steps promptly toward its correction, by whatever method of group or individual instruction may prove necessary or advisable, but with special emphasis on ability to recognize at first letters and their phonetic values, and later the analytic details of syllable and word structure.

4. As regards many children, perhaps the great majority, it is probable that an important mistake has been made, for the past quarter century or more, in too wide a departure from the old more or less mechanical methods of teaching word structure and recognition. The most practical approach to educational economy in acquirement of the reading skill includes not merely an attempt to correct failures already more or less firmly established but the use of teaching method which will as far as possible avoid creation and fixation of reading failures in each new school generation.

1276 Emerson Street (3).

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1. Toward Better Reading (intended for Denver high schools).
2. Reading Guide (for use in the elementary school).

STUDIES OF THE EYE IN OLD AGE*

II. Hole in the macula: A clinico-pathologic study

A. L. Kornzweig, M.D., and Morris Feldstein, M.D.
New York

The pathogenesis of cysts and holes in the macula has been well summarized by Duke-Elder[1] and Elwyn.[2] The original reports of Blessig[3] and Ivanoff[4,5] stressed the process of cystoid formations in the retina, referring especially to those near the ora serrata. The formation of cysts and holes in the macular region has been discussed by Noyes,[6] Haab,[7] Kuhnt,[8] Fuchs,[9] Pagenstecher,[10] Dufour and Gonin,[11] Reis,[12] Purtscher,[13] von Szily,[14] and Lister.[15] They all stressed the role of trauma and contusion to the eyeball as a contributory and etiologic factor. Nontraumatic holes in the macula are much less common, only 3 in 27 cases of the Haab[7] and Ogilvie[16] series.

The causes of cysts and holes in the macula of the nontraumatic type are believed to be due to degenerative changes, the aging process, chorioretinitis, pigmentary degeneration of the retina, renal retinopathy, and detachment of the retina. Toxins liberated by inflammation in the anterior segment of the eye are also included as causative factors by Fuchs,[9] de Schweinitz,[17] Zeeman,[18,19] Vogt,[20] Arnold,[21] Samuels,[22] and Wolff.[23]

The process whereby cystoid spaces are first produced in the outer plexiform layer of the retina and then enlarge and coalesce, gradually leading to a complete breakdown of the tissue and the formation of a hole, has also been fully understood and described by the many writers on this subject, especially in the interesting and exhaustive papers of Coats,[24] Zeeman,[18,19] and Samuels.[22] Most of the pathologic reports, however, are based on eyes that were removed for other causes, such as prolonged inflammatory disease, phthisis bulbi, tumor, or severe injury.

In the case to be reported, both eyes were obtained shortly after death and were free from other pathologic lesions. Since this case presented unusual opportunities for clinical and pathologic correlations, and seemed to clarify the problems of pathogenesis, it is deemed worthy of report in detail.

Case report

History

The patient, N. C., a man, aged 64 years, was admitted to the Home for Aged and Infirm Hebrews in July, 1946. The diagnosis on admission was hypertension, bronchial asthma, generalized arteriosclerosis, and arteriosclerotic heart disease. An X-ray study of the chest, taken at that time, revealed pulmonary congestion, early bronchiectasis of both lower lobes with chronic pneumonitis. The blood sugar was 83 mg. percent, and the blood urea, 14.8 mg. percent. The asthmatic attacks were later considered to be cardiac in origin.

On December 19, 1946, an eye examination was done. The vision in the right eye was 20/40 with correction. The vision in the left eye was finger-counting at two feet and could not be improved. The lids were normal. The conjunctivas were moderately injected and slight epiphora was present. Pupillary reactions to light and accommodation were normal. The media were clear.

The right fundus showed a normal optic disc. The arteries were tortuous and narrowed. The macular region was stippled,

* Presented before the New York Society for Clinical Ophthalmology, February 7, 1949. From the Ophthalmological Service of the Home for Aged and Infirm Hebrews of New York City. This study was made possible by a grant from the Research Fund of the Home for Aged and Infirm Hebrews. The first study on this series, "Occlusion of the central retinal artery," appeared in the American Journal of Ophthalmology, 31:1421 (Nov.) 1948.

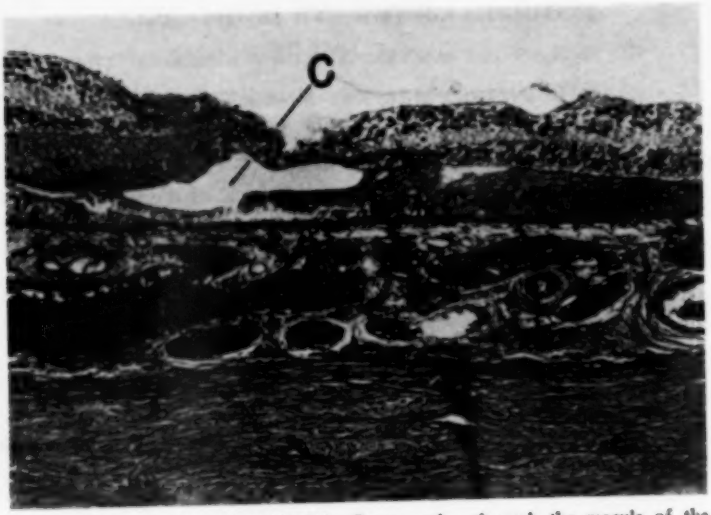

Fig. 1 (Kornzweig and Feldstein). Cross section through the macula of the right eye. The clear area (C) is the peripheral part of the cystoid degeneration. It involves chiefly the outer plexiform layer, and part of the outer and inner nuclear layers. The ganglion cell layer is thinned, and the internal limiting membrane is frayed.

Fig. 2 (Kornzweig and Feldstein). Cross-section through the macula of the right eye. The cystoid area (C) is much larger. All the layers are involved, except the outer limiting membrane and the cone processes. The inner wall of the cyst is a thin strand of tissue at the level of the internal nuclear layer. The internal limiting membrane, the nerve-fiber and ganglion-cell layers are missing internal to the inner wall.

Fig. 3. (Kornzweig and Feldstein). Cross section through the macula of the right eye. The inner wall of the cyst is ruptured. All that remains to convert the cyst into a hole in the macula is the atrophy of the outer limiting membrane and the remnants of the cone processes.

but otherwise normal. No hemorrhages or exudates were present. In the left eye, the disc was normal and the arteries showed the evidence of arteriosclerosis, namely, narrowing, alteration of caliber, and increased tortuosity. In the macular region a large, well-defined hole was seen, measuring almost one-half the diameter of the disc, and surrounded by small areas of yellowish exudate.

Shortly thereafter, the patient's general condition deteriorated, and he became a permanent infirmary case with constant dyspnoea. He was maintained on digitalis therapy with occasional injections of mercurial diuretics. In November, 1947, he developed bronchopneumonia and died on November 21, 1947.

Postmortem findings

1. Pulmonary embolism to the right middle and right lower lobes with infarction.
2. Hemorrhagic bronchopneumonia, right middle lobe.
3. Acute fibrinous pleuritis, right middle lobe, right lower lobe.
4. Marked pulmonary emphysema.
5. Patchy pulmonary atelectasis and congestion.
6. Arteriosclerotic coronary heart disease: (a) Old myofibrosis with aneurysm formation of the posterior wall and septum of the left ventricle; (b) marked hypertrophy and dilatation of both ventricles; (c) marked calcific coronary arteriosclerosis with narrowing.
7. Moderate aortic arteriosclerosis.
8. Congestion of the liver, spleen, and kidneys.
9. Acute hemorrhagic cystitis.

Both eyes were removed at the time of autopsy, 10 hours after death. They were placed in Bouin's solution and prepared in the usual way. They were embedded in paraffin, however, and stained with the Mallory trichrome technique. Numerous sections through the macula in each eye were made.

Pathologic report

The right eye shows a large cystoid degenerative area in the macular region (Figs. 1, 2, and 3). Almost all the layers of the retina are involved. Still intact is the outer limiting membrane with a few cone processes attached to it. The widest part of the cyst is in the external plexiform layer. The internal nuclear layer is still continuous through a narrow strand of tissue, which is ruptured in one section. The internal limiting membrane can be identified up to the margin of the cyst and then disappears. No fluid or debris is seen in the cyst cavity.

The left eye shows a complete gap of all the layers of the retina in the macular region (fig. 4). This is the true hole in the macula and it measures 0.7 mm. in diameter. The edges of the retina surrounding the hole are rather sharply defined and rounded. The retina beyond the hole is fairly normal; a few small spaces are seen in the external plexiform layer. There is a space between pigment layer and retina which would appear to indicate the presence of a detachment in this region, but this may be an artefact. The pigment layer is intact throughout. The choroid is normal, the arteries show a moderate degree of thickening of the media, but the endothelial lining of the blood vessels is intact.

Discussion

There are several interesting points deserving of comment.

The right eye, at the time of examination, 11 months before death, had a vision of 20/40 with correction. Stippling of the macula was noted, but there was no evidence of cystic degeneration. Fundus examination with red-free light, as recommended by Vogt,[20] was not done. In the interval between the examination and death, the macular region had undergone this rather marked cystoid degeneration, just short of complete disintegration, with the formation of a hole.

The left eye, which already had a hole in the macula, had remained stationary. The

surrounding retina showed none or very slight evidence of deterioration. There was no history of injury or inflammation in either eye, before or during the stay in the hospital. The patient did, however, have numerous asthmatic attacks, and suffered from cardiac decompensation in the last few months of life.

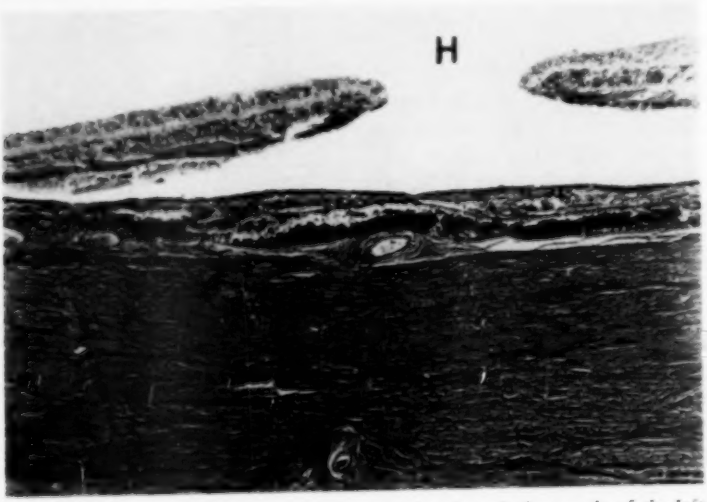

Fig. 4 (Kornzweig and Feldstein). Cross section through the macula of the left eye. There is a complete gap in the retina, involving all the layers, forming a true hole in the macula (H). The edges of the hole are rounded, due to shrinkage and traction on the internal limiting membrane which pull it outward until it is almost continuous with the external limiting membrane. The neighboring retina appears to be intact, except for some small spaces in the external plexiform layer that may be artefacts. The pigment layer and choroid are normal.

The sharp, rounded margins of the hole in the left macula were caused by shrinkage and traction on the internal limiting membrane which pulled it outward until it was almost continuous with the external limiting membrane. This traction was exerted undoubtedly through Mueller's fibers which unite the two limiting membranes. The retinal circulation, which was inadequate for the macular region, was just sufficient to maintain normal nutrition in the paramacular area. This accounts for the relatively healthy region around the tear. The pigment layer, choriocapillaris, and choroid immediately subjacent to the hole were intact. One is led to believe that the nutrition to the macular region is dependent almost entirely upon the retinal circulation.

This occurrence of a cystoid degeneration in one eye and a hole in the macula of the other eye of the same patient has been noted clinically, but has not been reported pathologically. To our knowledge, this is the first such report, and it tends to corroborate the theory of the interrelation of these two pathologic processes. Cystoid degeneration precedes the formation of hole in the macula. In this patient this process is secondary to local and general vascular change superimposed possibly on the changes of senescence. No evidence of inflammatory disease was seen around the macula or in the anterior segments of the eye. There is no sign of injury to either eye.

The two areas of the retina most prone to cystic changes are the macular region and the ora serrata. In these places the retinal circulation is poorest and hence the tissues

are most readily affected by local and general bodily changes which impair the circulation and cut down nutrition to the affected areas. It is assumed that these changes are secondary to the gradual obliteration of the small retinal arterioles which supply these regions, as described by Vogt and stressed by Elwyn.

Such obliterated vessels were, however, not seen in these sections. Whether this is a purely fortuitous occurrence which happens to affect the arterioles in the macular region, or whether it is due to an inherent predisposition to such change, is not known. Certainly the frequency with which hole in the macula occurs in both eyes would tend to favor the latter theory.

The value of routine postmortem examination of the eyes of the aged is emphasized by this paper. The usual and the unusual findings in the eyes of old people may thus be studied and correlated with clinical observations. Such a project has been under way in this institution for the past four years. The observations made on the first 100 cases will form the subject of a report now in preparation.

Summary

Clinical and pathologic studies of the eyes of a 64-year-old man are herewith presented. Simultaneous occurrence of hole in the macula in the left eye and cystoid degeneration of the macula in the right eye is described and discussed as to cause, pathogenesis, and relation to general bodily changes.

1200 Fifth Avenue (29).

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HOLE IN THE MACULA

LEO J. CROLL, M.D., AND MAURICE CROLL, M.D.
Detroit, Michigan

Ivanhoff, in 1865, first described cystoid spaces as arising where the supporting structure of the retina is the weakest, that is, in the inner portion of the outer nuclear layer and in the inner nuclear layer. The cysts arise by rarefaction of the nervous elements of the retina and are usually associated with changes in the capillaries.

Cystic degeneration may occur anywhere in the retina, but it has a special predilection for the periphery of the retina and the macula because these two areas are the thinnest anatomically and are comparatively poorly vascularized. The cystic spaces, which are full of edematous fluid, are formed in the macular, retinal layers. When the cysts rupture, they produce a depression in the central area and, if the entire thickness of the retina is involved, a complete macular hole is formed. The usual sequence of events in delayed formation of hole in the macula is early evidence of edema, cystic degeneration of the macula, rupture of the cysts, and hole formation at the macula.

Verhoeff states that hole in the macula is always preceded by cystic degeneration. Samuels says that a special type of cavity develops at the fovea because there are no supporting fibers of Mueller to confine the edematous fluid and that the result is the formation of large globular cystic lesions at the macula. The macular region is the most delicate, the thinnest, and the most highly organized area of the retina, and these characteristics make it extremely susceptible to edema and cystic formations.

The hole at the macula is usually about one-third to one-half the size of the disc. The retinal vessels exhibit varying degrees of arteriolar spasm. This is evidenced by localized constrictions with reduction of the lumen of the vessels to about one third of their normal size. The ratio between arterioles and veins is about 1:3 and is evidenced by a narrowing and increased brilliancy of the central light reflex stripe.

The escape from the circulation of fluid causing edema is usually an indication of endothelial, capillary, or tissue damage. When the capillary permeability is increased, edematous fluid escapes to the tissue. This leads to the formation of exudates and eventually to the escape of formed elements of the blood in the form of hemorrhages. Early changes of this type are reversible, but the later, more advanced changes are not reversible.

The edematous process is usually first seen in the nerve-fiber layer where the majority of blood vessels lie. The nerve fibers are surrounded by potential spaces which readily become edematous. Cystic spaces appear readily in the ganglion-cell layer, pushing the ganglion cells into the distended spaces, and this development is the forerunner of formation of hole in the macula.

In injuries to the eye such as contusions, perforations, wounds, and contrecoup, the macula and fovea are the most vulnerable. Traumatic edema of the retina or (commotio retinae) is the result of sudden violent force transmitted from the anterior segment of the globe to the posterior pole. In this condition the macular area becomes milky gray with a redder area at the center. The radiating circular light reflex around the macula is indicative of the presence of edematous fluid under the internal limiting membrane. When a hole is formed, it gives a punched-out appearance so that the dark red granular choroid is ophthalmoscopically visible.

Duke-Elder states that edema following contusions to the globe depends upon sudden vasoconstriction followed by extreme vasodilatation. It is always most pronounced at the macula, where it is typified in traumatic retina, an edematous condition which clears up after a few days.

Our experience in an Army general hospital and eye center where patients with more severe trauma (due to high-speed velocity missiles) were seen, differs from Duke-Elder's. In our cases, the edema around the macula did not readily clear up. According to the many field records we have reviewed, these patients were seen immediately after injury and did not then have a hole in the macula; instead they had edematous retinas with fair vision ranging from light perception to 20/40. Eventually, in from 1 to 4 months, they developed complete hole in the macula and of course had only peripheral vision.

After reviewing the field records and examining many patients who had suffered war and bombing injuries to the eyes, we were impressed with the frequency of edema of the retina and spasm of the retinal vessels. It seemed to us that these cases could be classified as vascular injuries.

When the eyeball and the retinal vessels are subjected to direct trauma, contusions, or the near impact of explosive fragments, the retinal vessels go into spasm and may keep up the spasm for many hours, even many days. The retinal arterial spasm so induced is usually quite severe. We have observed marked attenuation of the blood column in the retinal arterioles and, in a few patients, the main large arteries appeared as fine thin strings 3 or 4 months after injury.

Patients who immediately after injury show hole formation at the macula cannot be helped. But patients with edema of the retina following injury may develop hole in the macula at a later time. These patients should be given the benefit of intense vasodilatation therapy in an attempt to prevent complete hole formation at the macula.

Salzman, in 1919, found eight patients with holes in the macula among 2,400 war injuries. We have seen 14 patients with complete hole formation among 3,600 war injuries. We have also seen eight patients with delayed hole formation at the macula and preservation of partial, useful central vision among 3,600 war injuries.

In 10 of the 14 patients who had an immediate complete hole at the macula, concussion blast was the cause. (Lagrange, cited by Doherty, defines "blast" as a disturbance of atmospheric pressure in the neighborhood of detonation of a high explosive missile. Two phases are present, a sharp phase of positive compression which is followed by a larger phase of rarefaction or negative pressure.)

The other four patients with immediate hole formation at the macula received severe unilateral wounds of the facial bones, and the eye injury was always on the same side as the facial injury. In these cases there was an accompanying traumatic chorioretinitis, also on the same side as the injury. One case of bilateral hole formation at the macula was seen. This was in an airman who made a forced landing.

Case reports

Two of the eight patients with delayed hole formation and three of the 14 with immediate hole formation are being reported.

Case 1

History. On November 29, 1944, while in action near Aachen, Germany, H. R., a 29-year-old sergeant, sustained injuries to the right cheek and fracture of the right zygomatic arch when an 88-mm. enemy shell exploded close by. Immediately following injury, he complained of blurred vision in his right eye. This patient was returned from the E.T.O. four days after his injury.

Ophthalmic examination showed the anterior segment to be clear, but fundus examination disclosed an edema of the macula with a radiating, circular reflex around the macula.

Vision was: O.D., 20/400, J7, not correctible; O.S., 20/30, J1, correctible to 20/20, J1. The patient was immediately given vasodilators and, in about one month,

vision in the right eye had improved from 20/400 to 20/60.

After about four months of vasodilator therapy, the edema of the macula subsided, but the macular area showed increased pigmentation. At this time, no spasm of the retinal vessels was seen. Visual images, however, appeared smaller in the right eye. Micropsia, a common occurrence with macular damage, is caused by separation of the visual elements.

If this patient had not received prompt vasodilator therapy, a complete hole formation might have developed at the macula.

Fig. 1 (Croll and Croll). Complete hole in the macula, immediate formation.

CASE 2

History. C. J. J., a first lieutenant, aged 24 years, was injured in France on July 28, 1944, when his jeep struck a land mine. He suffered multiple injuries and fracture of the left facial bones and zygomatic arch.

Ophthalmic report. L.E.: Vision was 20/200, J7. There was commotio retinae and marked edema around the macula. The right eye was normal in all respects.

Vasodilator therapy was started immediately and continued for about 30 days. When seen 89 days after injury, vision in the left eye was 20/70, J6, correctible to 20/20. The macula showed a sharply outlined area, about one-third the size of the disc, and disorganization of the macular pigment. There was slight constriction of the superior and inferior macular vessels.

Although this patient may develop a complete hole in the macula, early and intensive therapy with vasodilators has improved metabolism of the macular area and has delayed hole formation at the macula.

CASE 3

History. A 29-year-old white private was in a slit-trench near a pillbox near Aachen, Germany, on October 6, 1944, when an enemy mortar shell hit the pillbox. He sustained injuries to the right eye, right shoulder, and right jaw.

Eye findings. After evacuation to the United States, an 0.5 by 0.5 by 0.5 mm. magnetic foreign body was removed from the sclera under the insertion of the internal rectus muscle. Vision in the right eye was 6/400, not correctible.

The vitreous was cloudy due to hemorrhage. There was a sharply outlined, circular, dark-red spot at the fovea and a punched-out hole at the macula. The hole was about one-fourth the size of the disc and was surrounded by an indistinct halo with radiating white streaks, indicating edematous fluid.

This hole at the macula appeared immediately following injury. The edema around the macula persisted for about four months. The superior and inferior vessels

were constricted. The left eye was normal in all respects.

CASE 4

History. On August 15, 1944, this white soldier, aged 25 years, suffered penetrating wounds of the face and right eye when his landing craft struck a land mine, near Toulon, France. He was transferred to the 21st General Hospital where vitreous hemorrhage and hole at the macula were recorded. He was immediately evacuated to the Zone of the Interior.

Ophthalmic findings. Vision was: O.D., 10/200, J0, not correctible; O.S., 20/20, J1, normal in all respects.

Heavy, fluffy exudates due to hemorrhage were present in the vitreous of the right eye. At the macula, there was a hole about one-third the size of the disc. The dark-red, granular surface of the choroid was readily seen. The edges of the hole were clear, distinct, and surrounded by a circular light reflex, indicative of edematous fluid.

Five months later the edema still persisted. The superior and inferior macular vessels were markedly attenuated, probably the result of persistent spasm. Vasodilator therapy was instituted and the edema disappeared in two weeks.

CASE 5

History. While in Germany, on September 17, 1944, this white soldier, aged 32 years, was injured when an 88-mm. shell exploded close to him. He immediately complained of blurred vision in the right eye.

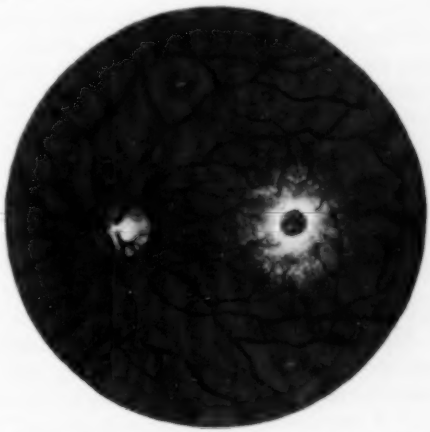

Fig. 2 (Croll and Croll). Hole in the macula, delayed formation, giving a cystic appearance.

Ophthalmic examination. Vision was: O.D., light perception and projection, not correctible; O.S., 20/20, normal in all respects.

There was a hole in the macula of the

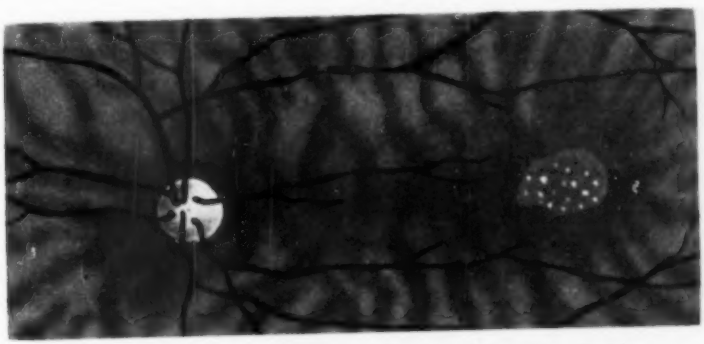

Fig. 3 (Croll and Croll). Hole in the macula, a large, delayed, and uneven formation of cystic spaces.

right eye with a circular dark area about one-third the size of the disc. Surrounding the hole was a radiating, circular light reflex indicative of edema of the retina at the macula.

Four months after injury, the edema still persisted. Vasodilator therapy was started, and the edema subsided in three weeks. The inferior and macular small vessels were attenuated.

Comments

In the 22 patients who suffered retinal damage, no retinal detachments were seen and only one instance of bilateral hole at the macula was observed.

Therapy

The vasodilator treatment given to these patients varied considerably. However, the therapy carried out at the eye center was:

1. A psychiatric consultation was obtained and an attempt was made to allay the soldier's fears.
2. Phenobarbital (0.5 gr., 3 times daily) was given.
3. No smoking. This rule was rigidly enforced.
4. Erythrol tetranitrate (Merck) (0.5 gr. every four hours) was given in an attempt to get a mild, gradual, prolonged vascular dilation.
5. Nitroglycerine (1/100 gr. under the tongue twice daily) was ordered.
6. Sodium nitrate (100 mg.) was administered by subcutaneous injection.
7. Typhoid vaccine was given in small doses, 10 to 15 million organisms, by vein every third day, causing a slight rise in temperature and subsequent vasodilation of peripheral vessels.
8. Ten cc. calcium gluconate (10 percent) were given daily for the first seven days because calcium is said to decrease the permeability of the capillaries.
9. Atropine sulphate (1 percent) was administered twice daily to keep the eye at rest and for better observation of the fundi.
10. Histamine was given in an attempt to obtain more prolonged vasodilation and more rapid improvement. Histamine (0.275 mg. of histamine diphosphate) is placed in 250 cc. of normal saline, and given intravenously very slowly, 16 to 18 drops per minute, so that it takes about four hours to give the 250 cc. If it is given too rapidly the patient will complain of headache. On slowing up the rate of infusion, however, the headache readily disappears.

Blood pressure readings were taken before histamine was administered and every half hour while giving it. Although all of the patients stated that they could see better, there was no demonstrable change in the fundus picture. Histamine was given twice weekly to the patients for 6 to 8 weeks, as deemed necessary.

The entire treatment as outlined was carried out for a minimum of two months and a maximum of three months. Prolonged and constant vasodilation is difficult to obtain and probably not desirable unless it can be well controlled.

Cystic formation at the macula, without rupture and with no hole formation, gives rise to distorted images. All patients who have been exposed to severe blasts are examined for evidence of micropsia and macropsia, by having them look at a dot placed in the center of a staff of parallel lines.

Conclusions

1. Fourteen cases of complete hole formation of the macula were seen among 3,600 war casualties.
2. Eight cases of delayed hole formation were seen among 3,600 war casualties and all of them have retained useful vision to date. All of the eight patients received vasodilator therapy.
3. Two cases of delayed hole formation and three cases of complete hole at the macula are reported. These patients received intensive vasodilator therapy.
4. One case of bilateral macular hole was seen.

1326 Maccabees Building (2).

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THE HISTOCHEMICAL LOCALIZATION OF CHOLINESTERASE IN OCULAR TISSUES*

GEORGE B. KOELLE, PH.D., AND JONAS S. FRIEDENWALD, M.D.
Baltimore, Maryland

In a previous publication,[1] we have reported a histochemical method for localizing cholinesterase activity in tissues. The substrate employed, acetyl-thiocholine, was found to be hydrolyzed by both specific and nonspecific cholinesterases at a greater velocity than acetylcholine; therefore, the sites of both types of enzyme are visualized.

Frozen sections or teased muscle preparations are incubated for varying periods in a medium containing acetyl-thiocholine (0.004 M.) and copper glycinate (0.002 M.), buffered to a pH of approximately 8.0 and saturated with copper thiocholine.

As the substrate is hydrolyzed to thiocholine by the cholinesterases present, copper thiocholine is precipitated, which is converted to copper sulfide by subsequent treatment with ammonium sulfide. The amorphous dark brown deposits of copper sulfide thus indicate the presumptive sites of enzymatic activity. In control preparations previously treated with 0.001 M. di-isopropyl fluorophosphate, an irreversible cholinesterase inhibitor, the typical staining does not appear. Findings in several mammalian tissues were described and illustrated.

* From The Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital. This work was supported by the National Institute of Health, John and Mary Markle Foundation, and Chalfant Fund. Presented at the 18th scientific meeting of the Association for Research in Ophthalmology, Philadelphia, June, 1949.

EXPERIMENTAL STUDY

This technique has proven unsatisfactory for the ciliary body and retina of the albino rabbit because of their greater friability. The following modification has therefore been employed in the present study.

Immediately after killing the animals by the intravenous injection of air, the eyes were enucleated and bisected sagittally. The retinas and the ciliary bodies were carefully separated from the surrounding tissues, leaving the iris attached to the latter. The retinas were cut with fine scissors into strips measuring approximately 3 by 10 mm.; radial segments of the ciliary body and iris were similarly prepared. These portions of tissues were then treated in the same manner as were frozen sections in the original method.

Incubation in acetyl-thiocholine was extended to periods of 1 to 3 hours, and after being rinsed and treated with $(NH_4)_2S$, the tissues were fixed in formalin, dehydrated, and sectioned in paraffin at seven micra. Sections were mounted both without counterstaining and after counterstaining with hematoxylin-eosin or eosin alone. Although the prolonged incubation periods permitted a greater degree of autolysis to occur, the architectural structure of the tissues was fairly well preserved.

In the retina (figs. 1 and 2), cholinesterase activity appeared to be greatest in the inner

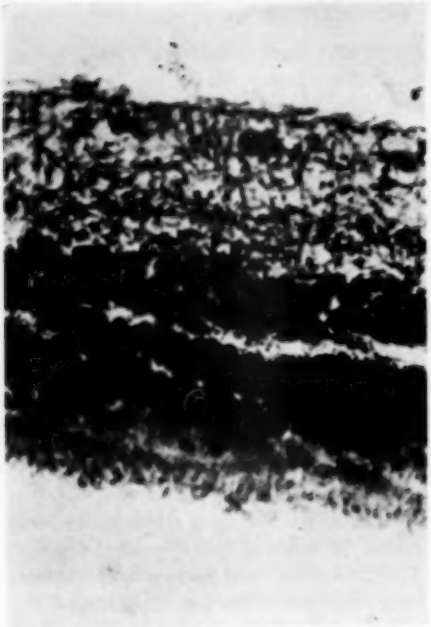

Fig. 1 (Koelle and Friedenwald). Retina, counterstained with hematoxylin-eosin (×600).

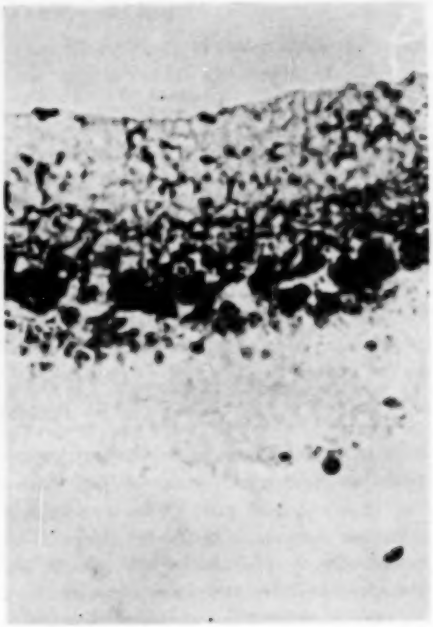

Fig. 2 (Koelle and Friedenwald). Retina, no counterstaining (×600).

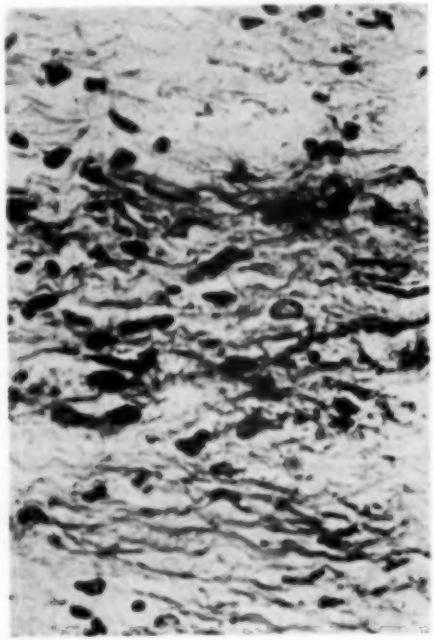

Fig. 3 (Koelle and Friedenwald). Ciliary muscle, no counterstaining (×600).

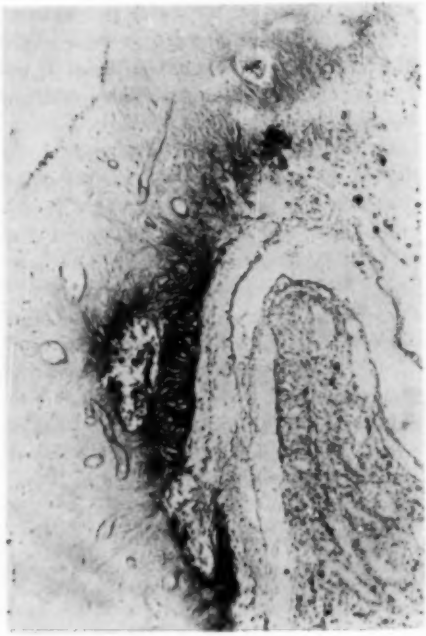

Fig. 4 (Koelle and Friedenwald). Base of iris, no counterstaining (×125).

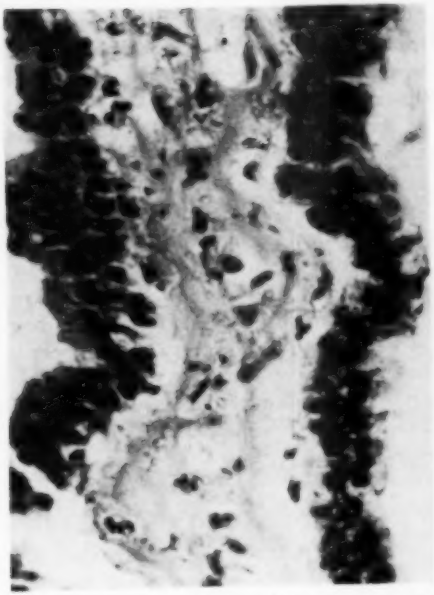

Fig. 5 (Koelle and Friedenwald). Ciliary process, counterstained with hematoxylin-eosin (×600).

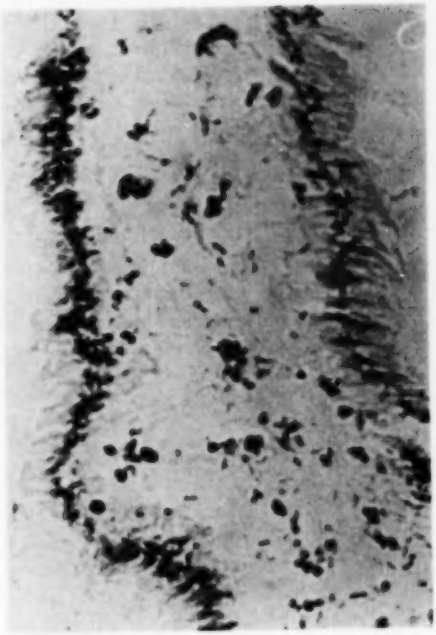

Fig. 6 (Koelle and Friedenwald). Ciliary process, no counterstaining (×600).

nuclear layer and the immediately adjacent portions of the plexiform layers. The heaviest concentrations were noted in the horizontal and bipolar cells. Evidence of isolated centers of enzyme activity was noted in the remainder of the plexiform layers and around the ganglion cells.

Sections of the ciliary muscle (fig. 3) revealed diffuse staining of the muscle fibers and their nuclei. The fibers on the posterior surface of the iris (fig. 4) and in the walls of the vessels were heavily stained (fig. 4). In the ciliary processes (figs. 5 and 6), cholinesterase activity appeared to be concentrated between the two layers of the epithelium, suggesting that the enzyme might play some role in the secretory process. The heavy precipitate noted throughout the stroma and within the vessels in the ciliary muscle apparently represents whole and fragmented erythrocytes, which are known to contain specific cholinesterase.

Studies are being conducted at present to distinguish between specific cholinesterase and nonspecific esterases at these and other locations.

The Johns Hopkins Hospital (5).

Reference

1. Koelle, G. B., and Friedenwald, J. S.: A histochemical method for localizing cholinesterase activity. Proc. Soc. Exper. Biol. & Med., 70:617, 1949.

Discussion

Dr. David Cogan (Boston): At one time previously, when I had occasion to talk with Dr. Koelle, I mentioned the apparent contradiction between what he found and what

Anfinsen found when he determined cholinesterase by a different technique.

I would be interested in asking Dr. Koelle if he can resolve this apparent contradiction.

DR. KOELLE: Would you mind repeating what that contradiction was?

DR. COGAN: Anfinsen, whose papers we cited to you a few months ago, had used quite a different technique in determining cholinesterase, and found it was concentrated or represented almost exclusively in the internuclear layers, and was not present in the nuclear layers of the retina. He concluded that it was localized at the synapsis, just contrary to what you find.

As I understand it, your localization is in the nuclear layers of the retina.

DR. GEORGE B. KOELLE (Baltimore): Anfinsen (J. Biol. Chem., 152:267, 1944) determined the localization of cholinesterase in the retina by subjecting horizontal sections to histologic analysis and titrimetric assays of enzyme activity. By this procedure he was able to show that the outer nuclear layer was devoid of significant cholinesterase activity, which is in keeping with our present findings. However, he was unable to obtain direct data on the activity of the inner nuclear layer since, as he stated, this layer was too thin to permit the isolation of cytologically homogeneous material. All his determinations on sections which included this layer showed high cholinesterase activity. Although he concluded the activity probably resided primarily in the adjacent synaptic layers, Anfinsen's results do not exclude the possibility of the inner nuclear layer's also possessing high cholinesterase activity.

The three-hour incubation period used in the present technique undoubtedly permits a marked degree of autolysis with consequent disruption of the normal architectural pattern. It is conceivable that the synaptic regions in our tissues may have been partially destroyed and therefore appear to have less enzyme activity than is actually present. I think it is quite possible that the localization of cholinesterase activity is primarily in the region of the synapses, which raises the question as to where most of the synapses actually lie—out in the plexiform layers or in the immediate region of the bipolar cells.

DR. COGAN: Anfinsen's localization was between the nuclear layers. He inferred they were synapses, but they were internuclear rather than nuclear.*

* Subsequent to the above discussion, we have repeated the studies on the rabbit retina using a shorter incubation period (two hours). In the sections so obtained, cholinesterase activity was noted in both the inner and outer plexiform layers (more marked in the former), but again appeared to be highest in the region of the bipolar cells. George B. Koelle.

DEHYDROASCORBIC ACID—ASCORBIC ACID IN THE AQUEOUS HUMOR OF RABBITS*

V. Everett Kinsey, Ph.D.
Boston, Massachusetts

The concentration of ascorbic acid in the aqueous humor is more than 10 times that in the blood plasma, indicating that a secretory process is involved in maintaining the concentration gradient. Inasmuch as the level of this compound in the aqueous humor has been reported to be low when the lens is removed or damaged,[1] the suggestion has been made that it is the first oxidation product of ascorbic acid (dehydroascorbic acid) which is secreted into the intraocular fluid rather than ascorbic acid itself, and that the dehydroascorbic acid is reduced to ascorbic acid by the lens.[2] The postulated transport mechanism for the dehydroascorbic acid is that the ascorbic acid from the blood is oxidized on the stromal side of the secretory boundary of the ciliary body from where it diffuses into the posterior chamber. Indirect evidence has been adduced from the role which ascorbic acid is thought to play in the secretion of aqueous humor by the ciliary body.[2]

Dehydroascorbic acid is readily oxidized at body pH; however, there is considerable question as to the exact nature of the oxidation products. Ball[3] has reported that dehydroascorbic acid has a half life of approximately two minutes at 37°C. and at body pH. Penny and Zilva[4] reported that dehydroascorbic acid at pH 7.4 becomes irreversibly oxidized to 2,3 diketogulonic acid with a half life of less than eight minutes, and the 2,3 diketogulonic acid itself is destroyed at a rate corresponding to a half life of approximately 100 minutes. These observations suggest that, if ascorbic acid in the aqueous humor comes from dehydroascorbic acid, it may not represent all of the dehydroascorbic acid transferred, but only a fraction thereof, and also that appreciable quantities of further oxidation products of ascorbic acid should be demonstrable in the aqueous humor.

While the magnitude of this fraction would depend upon the rate at which dehydroascorbic acid could be reduced to ascorbic acid, and also upon the diffusion rates in the posterior chamber and lens, the possibility that some compound may be secreted into the posterior chamber in unknown amounts is of considerable significance in attempting to account for the excess of osmotic pressure in the aqueous humor compared with the plasma.

In rabbits, the contribution to the osmotic pressure in the aqueous humor due to ascorbic acid is less than a millimol equivalent of sodium chloride. However, if the number of molecules of ascorbic acid reaching the anterior chamber were but a quarter of the total number of molecules secreted in the form of dehydroascorbic acid, the added solutes due to secretion of this acid alone would be approximately sufficient to account for the total excess osmotic pressure which has been observed.[5]

The same would hold true if the dehydroascorbic acid were secreted as an anion, it being apparent that since electrical neutrality must be maintained, an ion of the opposite charge would be moved across a barrier at the same time.

Therefore, it becomes important to the more general problem of aqueous-humor dynamics to determine the validity of the concept that it is dehydroascorbic acid which is secreted into the posterior chamber and subsequently reduced, presumably by the lens, to ascorbic acid. Accordingly, a study

* From the Howe Laboratory of Ophthalmology, Harvard Medical School. Supported in part by a grant from the Snyder Foundation. Presented at the 18th scientific meeting of the Association for Research in Ophthalmology, Philadelphia, June, 1949.

has been made of the chemistry of dehydroascorbic acid in the aqueous humor, with emphasis on its possible conversion to ascorbic acid.

Methods

Ascorbic acid was determined by titrating with 2,6 dichlorophenolindophenol in four-percent metaphosphoric acid, using pure ascorbic acid as a standard. A modified Rehberg burette having a volume of 0.00187 ml./division was used to deliver the dye. The error of titration in the quantities used was ± two percent.

Fig. 1 (Kinsey). Micropipette with jacket.

Dehydroascorbic acid was prepared immediately before use by oxidizing ascorbic acid with an equivalent amount of potassium iodate. The end point was checked on aliquots by the usual iodimetric analytical technique, or 2,6 dichlorophenolindophenol; the former was used also for glutathione analysis. When solutions contained ascorbic acid and glutathione, both of which react with iodate, the former compound was determined separately by rapidly titrating with the dye, and the quantity of glutathione present was determined by difference.

Dehydroascorbic acid was determined by bubbling moist hydrogen sulfide through the solutions for 15 minutes, removing the hydrogen sulfide by passing moist nitrogen for one hour, and determining the quantity of ascorbic acid produced by titrating with 2,6 dichlorophenolindophenol.

2,3 Diketogulonic acid was analyzed by the method of Penny and Zilva[8] which uses the amount of color formed with 2,4 dinitrophenolhydrazine under special temperature conditions as an index of the quantity of 2,3 diketogulonic acid present. On the premise that 2,3 diketogulonic acid should have an absorption peak at 290 mμ, other analyses were made using a Beckman spectrophotometer.

A sand bath, in conjunction with an air incubator, was used to minimize the temperature lag in the experiments in which a solution of dehydroascorbic acid was substituted for aqueous humor in beef eyes. The eyes were preheated by immersing up to the limbus in the sand. Water previously heated to 37°C. was used to prepare the dehydroascorbic acid solution. The sand bath and eyes were then all placed in the incubator at 37°C.

The samples of aqueous humor from the anterior chamber were taken by corneal puncture and those from the posterior chamber by a technique suggested by Dr. David Cogan, which consisted of inserting the needle of the micropipette (described below) through the sclera just behind the iris. The exact position of the needle could be determined by direct observation through the iris since albino animals were used. Blood entered the micropipette in only about five percent of the cases; in these instances the samples were discarded.

Because of the small amount of fluid (5 to 12 cu. mm.) which could be withdrawn, extreme care had to be taken to prevent evaporation of aqueous humor obtained from the posterior chamber. Special micropipettes and jackets (fig. 1) were constructed which made it possible to remove the aqueous humor and protect it from evaporation until it was delivered quantitatively into a container for analysis. The micropipettes were constructed as follows:

One hundred graduations at millimeter intervals (not shown in the figure) were marked on a six-inch piece of 1-mm. capillary tubing (7 mm. outside diameter) and the tube beyond the graduations was drawn to a taper. A No. 26-gauge needle was sealed into the tube with Glyptal, left to dry overnight at room temperature, and baked at 110°C. for 12 hours. The jacket was made from a glass tube having an inside diameter of 9 mm., the end of which was

also drawn out in such a way that the taper corresponded roughly to that of the end of the micropipette. The latter was then inserted into the jacket and an air-proof joint was formed by grinding the end of the micropipette into the end of the jacket with carborundum. When complete, the end of the jacket was sealed, allowing a millimeter or two clearance on the end for the needle. When the jacket is used, evaporation of water at room temperature from the end of the needle was less than 1 mg./24 hours; whereas, without the jacket it was 0.7 mg./minute. Relative humidity was approximately 30 percent (laboratory conditions in winter). The total volume of the micropipettes, between the zero and 100-graduation marks, was approximately 75 cu. mm., and 12 cu. mm. from the zero mark to the tip of the needle.* Gum rubber tubing was attached to the micropipette for delivering fluid.

Samples of aqueous humor were blown from the micropipette into micro tubes (4 mm. by 16 mm.), stoppered immediately with rubber caps, and weighed on an analytical balance having a sensitivity of 0.1 mg. Finger prints were removed by wiping with a clean, dry cloth.

Ascorbic acid and dehydroascorbic acid were injected into the posterior chamber of rabbit eyes using a different type of micropipette[7] in which pressure could be exerted by means of a tuberculin syringe affixed to one end. Paraffin oil was run in above the solution to be injected to make a solid column, since the cushioning effect of air lying between the liquid and plunger made it impossible to control exactly the amount of fluid to be injected. The volume of injected material was 2.5 cu. mm. and the injection was performed over a period of about 15 seconds; the eyes were proptosed while making the injection and were gradually permitted to assume their normal position in the orbit.

* The micropipettes and jackets, without needles, are now being made by Macalaster Bicknell Company, Inc., Cambridge, Massachusetts.

TABLE 1

THE CONCENTRATION OF SUBSTANCES IN AQUEOUS HUMOR OF RABBITS CAPABLE OF REDUCING 2,6 DICHLOROPHENOLINDOPHENOL BEFORE AND AFTER REDUCTION WITH HYDROGEN SULFIDE

Rabbit Number		Concentration—Ascorbic Acid Equivalent		
		Before Reduction	After Reduction	Difference
		mg. %	mg. %	Dehydroascorbic Acid? mg. %
1	O.S.	25.8	28.6	2.8
	O.D.	26.7	30.3	3.6
2	O.S.	22.3	25.7	3.4
	O.D.	21.8	25.0	3.2

EXPERIMENTAL

CHEMISTRY OF DEHYDROASCORBIC ACID IN THE AQUEOUS HUMOR

The first series of experiments was concerned with the determination of the kind and quantity of compounds related to ascorbic acid found in the aqueous humor, and the rate at which dehydroascorbic acid becomes irreversibly oxidized in this fluid.

The concentration of dehydroascorbic acid in the aqueous humor was determined, it being assumed that any increase in reducing power after reduction with hydrogen sulfide was due to ascorbic acid formed as a result of reduction of dehydroascorbic acid. Table 1 shows that the reducing capacity of aqueous humor for 2,6 dichlorophenolindo-

phenol following reduction with hydrogen sulfide increases approximately 12 percent, which corresponds to approximately 3 mg. percent dehydroascorbic acid. This value is in agreement with results reported by Müller and Buschke.[1]

Analysis of aqueous humor for 2,3 diketogulonic acid by the analytical method of Penny and Zilva showed the presence of a substance, or substances, in the aqueous humor which would give a positive color test under conditions reported by these authors to differentiate 2,3 diketogulonic acid from ascorbic and dehydroascorbic acids. However, analyses by the same method on mutarotating solutions of dehydroascorbic acid under a variety of experimental conditions, failed to confirm similar work reported by Penny and Zilva.

This lack of agreement prompted the author to examine mutarotating solutions of dehydroascorbic acid spectrophotometrically, on the basis that while 2,3 diketogulonic acid has not been isolated so that its absorption spectra could be determined, it would be expected that this acid would have an absorption maximum at 290 mμ, since this is characteristic of diketones.

Absorption spectra were determined on mutarotating solutions of dehydroascorbic acid under various conditions as to pH, temperature, concentration, and so forth. An absorption maximum occurred at 290 mμ in solutions which were more acid than approximately pH 5, suggesting that 2,3 diketogulonic acid might well be one of the degradation products. When the mutarotation was carried out in phosphate buffer at body pH and temperature, the absorption maximum appeared at 270 mμ. Lowering the pH of the solution at the time of performing the analysis shifted the peak from 270 to 290 mμ.

It is sufficient to point out here that the peak at 270 mμ was not due to ascorbic acid. Moreover, it is noteworthy from the point of view of interpreting the positive test for 2,3 diketogulonic acid in the aqueous humor, as obtained by the method of Penny and Zilva, that the rate of appearance of the compound or compounds which gave absorption peaks at either 270 or 290 mμ did not correspond with increasing color formation as revealed by the method of Penny and Zilva. Hence, spectrophotometric analyses were made of aqueous humor.

Protein was first precipitated with zinc sulfate. The aqueous humor showed an absorption peak at 270 mμ, but unlike that obtained from mutarotating solutions of dehydroascorbic acid, the peak shifted to 250 mμ when the pH was lowered. This is characteristic of ascorbic acid. From these analyses it was concluded that aqueous humor does not contain appreciable amounts of 2,3 diketogulonic acid. Furthermore, chemical analyses indicated that the aqueous humor also contains no oxalic acid.*

Since the results of the analyses of aqueous humor failed to indicate the presence of appreciable quantities of any derivatives of dehydroascorbic acid, and only small quantities of the latter, it was thought worthwhile to redetermine the rate of oxidation of dehydroascorbic acid at body pH to ascertain if the rate was actually as high as earlier studies indicated. Samples were taken at intervals from mutarotating solutions of dehydroascorbic acid which were then reduced with hydrogen sulfide. Dehydroascorbic acid was said arbitrarily to be irreversibly oxidized when it could no longer be reduced to ascorbic acid.

Figure 2 shows that dehydroascorbic acid in phosphate buffer pH 7.3, and in beef aqueous humor, is irreversibly destroyed at rates corresponding to half lives of 22 and 50 minutes† in these solutions, respectively,

* Under alkaline conditions (pH 7.4) mutarotating solutions of dehydroascorbic acid are known to produce oxalic acid. This was confirmed by the present author who also noted apparently for the first time that furoric acid is one of the oxidation products of dehydroascorbic acid when mutarotation occurs under acid conditions.

† The rate was corrected for the amount of ascorbic acid present initially.

or about one third of that reported by Penny and Zilva.[4]

The present results suggest that conversion of dehydroascorbic acid to ascorbic acid by the lens would not have to be as rapid as previous work indicated and, at least so far as time is concerned, are compatible with the idea that reduction of dehydroascorbic acid may take place in the eye.

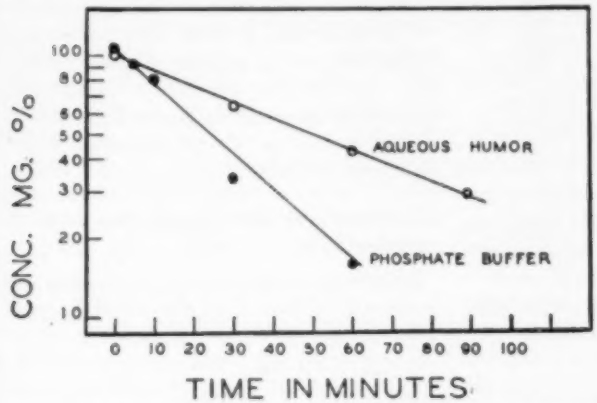

Fig. 2 (Kinsey). Irreversible oxidation of dehydroascorbic acid at 37°C. in phosphate buffer pH 7.3 (filled circles), and in aqueous humor (open circles).

Conversion of dehydroascorbic acid to ascorbic acid (in vitro)

The following experiments are concerned more directly with the reduction of dehydroascorbic acid to ascorbic acid.

The reduction of dehydroascorbic acid in the preceding experiment was carried out with hydrogen sulfide, a relatively strong reducing agent. Since it is presumed that any reduction of dehydroascorbic acid that may take place within the eye is due to glutathione, an experiment was performed to determine whether glutathione could reduce dehydroascorbic acid, and also the rate at which it might occur.

An amount of glutathione, chemically equivalent to the dehydroascorbic acid employed, was added to a freshly prepared solution of the latter and the concentration of ascorbic acid formed was determined from time to time. Figure 3 shows that glutathione can reduce dehydroascorbic acid and that the rate of reduction is such that approximately half the dehydroascorbic acid is reduced in approximately four minutes.

Having established that glutathione can reduce dehydroascorbic acid relatively rapidly, a similar test was made to determine whether the lens could accomplish the reduction. A whole beef lens was placed in 15 ml. of aqueous humor containing 100 mg. percent dehydroascorbic acid. Table 2, column 2, shows that the concentration of ascorbic acid in the solution actually decreased under these conditions.

A similar experiment was then carried out in which a crushed lens was substituted for the intact lens. Table 2, column 3, shows

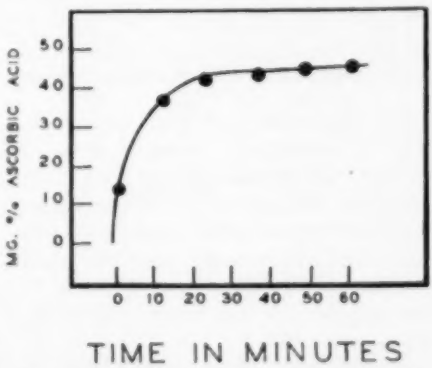

Fig. 3 (Kinsey). Conversion of dehydroascorbic acid to ascorbic acid by glutathione at 37°C., pH 7.3.

TABLE 2

REDUCTION OF DEHYDROASCORBIC ACID ADDED TO AQUEOUS HUMOR BY WHOLE AND CRUSHED BEEF LENS (37°C.)

Time (min.)	Whole Lens* mg. %	Crushed Lens† mg. %
0	10.5	25.9
10	9.7	41.5
20	8.7	48.0
30	8.0	50.6
60	5.5	50.8
90	3.7	54.3

* Volume solution 15 ml.; weight lens 2.3 gm.
† Volume solution 2.0 ml.; weight lens 2.2 gm.

that in this instance the concentration of ascorbic acid increased. The difference between these experiments would appear to be due to liberation of free glutathione from the crushed lens.

That this was the probable explanation may be seen from Table 3, in which the concentration of free glutathione in a solution of phosphate buffer containing a whole and crushed lens is compared.

Aqueous humor from a number of whole beef eyes was removed and replaced by a solution of dehydroascorbic acid made up in phosphate buffer. After 0, 3, 6, and 10 minutes of incubation at 37°C. the solutions were removed and analyzed for ascorbic and dehydroascorbic acids.

In no case was there a detectable amount of ascorbic acid present. The dehydroascorbic acid in the anterior chamber of the beef eyes became irreversibly oxidized at exactly the same rate as reported previously in this paper (fig. 2) for solutions of dehydroascorbic acid.

CONVERSION OF DEHYDROASCORBIC ACID TO ASCORBIC ACID (IN VIVO)

If dehydroascorbic acid were to enter the posterior chamber from the ciliary body, it might be expected that conversion to ascorbic acid by the lens would occur progressively as the aqueous humor passes through the iris/lens space, and thus the concentration

TABLE 3

AMOUNT OF ASCORBIC ACID AND GLUTATHIONE LIBERATED BY WHOLE AND CRUSHED BEEF LENS IN PHOSPHATE BUFFER (pH 7.3)

Time (min.)	Concentration in Solution*			
	Whole Lens		Crushed Lens	
	Ascorbic Acid mg. %	Glutathione mg. %	Ascorbic Acid mg. %	Glutathione mg. %
30	2.7	5.7	10.1	45.5
60	3.1	10.6	12.4	81.1

* Volume both solutions 2 ml.; weight lenses approximately 2 gm. each.

From the results shown, it is clear that not only is glutathione liberated from the crushed lens, but ascorbic acid is also freed. This later observation can in part account for the difference in the amount of ascorbic acid found initially in the experiment shown in Table 2, the values being 10.5 and 25.9 mg. percent for the whole and crushed lenses, respectively.

Another type of experiment was performed to test whether the intact lens could reduce dehydroascorbic acid to ascorbic acid. of ascorbic acid would be higher in the anterior than in the posterior chamber. To test this possibility, the concentrations of ascorbic acid in these parts of the eye were determined.

Results of 10 of these experiments are shown in Table 4, where it may be seen that the average concentration in the posterior chamber was 34 mg. percent; whereas, that in the anterior chamber was 25 mg. percent —actually a reversal of the expected result.

Since it may be argued that the experi-

mental procedure incident upon obtaining and measuring the samples from the posterior chamber may have influenced the results, the same technique was used to obtain aqueous humor from other rabbits, and the concentration of chloride was determined. The results, which will be reported in detail in another paper, show no significant difference between the concentrations of this ion in the aqueous humor taken from the posterior and anterior chambers.

Finally, 2.5 cu. mm. of a solution of neutralized dehydroascorbic acid were injected into the posterior chamber and after six minutes the concentration of ascorbic acid in the anterior chamber was determined.* The solution of dehydroascorbic

* Experiment suggested by Dr. Jonas S. Friedenwald.

TABLE 4

CONCENTRATION OF ASCORBIC ACID IN THE POSTERIOR AND ANTERIOR CHAMBERS OF THE RABBIT EYE

Column 1	Column 2*	Difference
Posterior Chamber mg. %	Anterior Chamber mg. %	Column 1 minus Column 2 mg. %
26	18	8
18	26	−8
26	19	7
34	23	11
44	18	26
51	35	16
33	35	−2
34	17	17
50	35	15
26	24	2
Av. 34.2	25	9.2

* Average of duplicate determinations.

TABLE 5

CONCENTRATION OF ASCORBIC ACID IN THE AQUEOUS HUMOR TAKEN FROM THE ANTERIOR CHAMBER OF THE RABBIT EYE FOLLOWING INJECTIONS OF 0.025 ML. OF:

A. Isotonic Dehydroascorbic Acid Solution (625 mg. %). Control Eye Injected with Physiologic Saline Solution

Concentration Ascorbic Acid				
	Injected Eye mg. %		Control Eye mg. %	Difference mg. %
+	27.5	0	27.2	0.3
0	29.9	++++	26.3	3.6
++	26.7	0	27.5	+ 0.8

B. Hypertonic Dehydroascorbic Acid Solution (1250 mg. %). Control Eye Not Injected

Concentration Ascorbic Acid				
	Injected Eye mg. %		Control Eye mg. %	Difference mg. %
+++	25.4	0	23.6	− 1.8
+++	17.5	0	19.5	+ 2.0
+++	21.2	0	24.7	+ 3.5

C. Hypertonic Ascorbic Acid Solution (1000 mg. %). Control Eye Not Injected

Concentration Ascorbic Acid				
	Injected Eye mg. %		Control Eye mg. %	Difference mg. %
++	100	0	24	+ 76.0
++	61	0	15.9	+ 45.1
++	129	0	29.9	+ 99.1
++	133	0	32.0	+ 101.0

* The 0 and + signs in Columns 1 and 2 refer to relative amount of protein present in sample.

acid was isotonic to the aqueous humor in three of the experiments, and hypertonic in three others. In three instances, an equal quantity of physiologic saline solution was injected into the control eye.

From Table 5 (parts A and B) it will be seen that there is no appreciable difference between the concentration of ascorbic acid in aqueous humor taken from the anterior chamber of the eyes which had been injected with dehydroascorbic acid, and either the uninjected eye or the eye receiving saline. As a control for these experiments an equivalent amount of ascorbic acid was injected into the posterior chamber and again the concentration of ascorbic acid was determined in the aqueous humor removed from the anterior chamber. Part C of the table shows that in this instance the concentration of ascorbic acid increased approximately fourfold.

Relation of dehydroascorbic acid in the plasma to that in the aqueous humor

On the basis of the more recent postulates of the mechanism of entrance of dehydroascorbic acid into the posterior chamber and its possible conversion there to ascorbic acid,[2] the amount of dehydroascorbic acid entering the aqueous humor would not be expected to depend upon the plasma concentration. Nevertheless, because of the failure of any of the experiments to show conversion of dehydroascorbic acid to ascorbic acid in the posterior chamber, it was thought of interest to learn whether the concentrations of ascorbic and dehydroascorbic acids in the aqueous humor were in fact dependent upon the concentration of dehydroascorbic acid in the plasma.

Incidentally, previous studies[8] had shown that within the range of plasma concentrations of 0.0 to 3.0 mg. percent, the concentration of ascorbic acid in the aqueous humor increased proportionately to that in the plasma, reaching a maximum value of approximately 50 mg. percent in the aqueous humor.

Two hundred milligrams of dehydroascorbic acid were injected intravenously into rabbits and the concentrations of ascorbic and dehydroascorbic acids were determined in the aqueous humor and plasma. The plasma concentrations of both acids increased (table 6); whereas, the concentration of dehydroascorbic acid in the aqueous humor was actually less than that found in a rabbit which had not been injected (table 1). No significance is attached to this observation.

The concentration of ascorbic acid in the aqueous humor rose (table 7) following intravenous injection of dehydroascorbic acid.

TABLE 6

Concentrations of ascorbic acid and dehydroascorbic acid* in the plasma and aqueous humor of rabbits following injection of dehydroascorbic acid made up in phosphate buffer (pH 7.3)

Time (min.)	Concentration—Ascorbic Acid Equivalent			
	Plasma		Aqueous Humor	
	Ascorbic Acid mg. %	Dehydroascorbic Acid mg. %	Ascorbic Acid mg. %	Dehydroascorbic Acid mg. %
0	1.25	0.21	—	—
33	1.67	0.76	—	—
65	2.09	0.81	—	—
243	1.88	—	—	—
315	—	—	26.1	0.2
320	1.67	0.28	—	—

* Difference between titration with 2,6 dichlorophenolindophenol before and after reduction with hydrogen sulfide.

TABLE 7

CONCENTRATIONS OF ASCORBIC ACID IN THE PLASMA AND AQUEOUS HUMOR OF RABBITS BEFORE AND AFTER INTRAVENOUS INJECTION OF DEHYDROASCORBIC ACID

Amount Injected mg.	Time (min.)	Concentration Ascorbic Acid	
		Plasma mg. %	Aqueous Humor mg. %
100	0	1.2	16.5
	58	1.9	28.5
200	0	0.6	11.9
	59	1.6	21.5

However, the rise in concentration is no more than would be expected from the increased concentration of ascorbic acid in the plasma, so does not, therefore, indicate that the concentration of ascorbic acid in the aqueous humor is directly dependent upon the concentration of dehydroascorbic acid in the plasma.

DISCUSSION

In so far as none of the experiments reported above supports the theory that dehydroascorbic acid enters the intraocular fluid from the blood and is subsequently reduced by the lens to ascorbic acid, the question of how to account for the low values for ascorbic acid in aphakic eyes arises. I have not been very successful in obtaining truly aphakic rabbit eyes, but in four eyes in which the lens had been partially removed at least, the concentration of ascorbic acid was found to be low only so long as there were signs of inflammation.

Since the iris-blood barrier is much more permeable during periods of inflammation, the low concentrations noted can be ascribed to loss of ascorbic acid from the anterior chamber to the blood by diffusion out of the eye, analogous to that postulated to occur in young animals through the hyaloid system.[9] It is not possible to state whether this explanation applies to previous results.

No explanation could be found to account for the different results obtained by Penny and Zilva. Recrystallization of various reagents gave identical results. The difference in rate obtained by Ball may have been due to the use of a dye intermediate by the latter worker. This may have catalyzed the reaction, thereby accounting for the more rapid rate of destruction of dehydroascorbic acid.

SUMMARY

Experiments were performed to determine the validity of the concept that the ascorbic acid in the aqueous humor enters the posterior chamber from the ciliary body as its first oxidation product; namely, dehydroascorbic acid, and is subsequently reduced to ascorbic acid by the lens.

In confirmation of work reported by others, evidence was obtained that normal rabbit aqueous humor contains approximately three mg. percent of dehydroascorbic acid. No oxidation products of dehydroascorbic, such as 2,3 diketogulonic or oxalic acids, could be detected in the aqueous humor.

The rate of irreversible oxidation of dehydroascorbic acid in phosphate buffer pH 7.3 and in aqueous humor was found to be sufficiently low (22 and 50 minutes, respectively) that presumably only a minor part of the postulated dehydroascorbic acid would be destroyed before it came into contact with the lens.

Dehydroascorbic acid was found to be reduced to ascorbic acid by solutions of glutathione or by crushed lenses, but not by intact lenses either in solution or in eyes which had been removed.

In rabbits, the concentration of ascorbic acid in the aqueous humor taken from the posterior chamber was 34 mg. percent, whereas that taken from the anterior chamber was 25 mg. percent. On the assumption that passage of fluid containing dehydroascorbic acid between the lens and iris was accompanied by reduction to ascorbic acid, this was contrary to expectation.

Injection of dehydroascorbic acid into the posterior chamber of eyes of living rabbits resulted in no increase in the concentration

of ascorbic acid in the anterior chamber. Injections of similar quantities of ascorbic acid resulted in a fourfold rise in concentration of ascorbic acid in the anterior chamber.

The concentration of dehydroascorbic acid in the aqueous humor did not increase following its intravenous injection. Increased concentration of ascorbic acid in the aqueous humor after such injections could be explained on the basis of the accompanying rise in the concentration of ascorbic acid in the plasma.

All of the evidence obtained is opposed to the theory that ascorbic acid in the aqueous humor enters the posterior chamber as dehydroascorbic acid to be subsequently reduced by the lens. It follows, therefore, that ascorbic acid itself is probably secreted by the ciliary body into the posterior chamber whence it flows with some loss into the anterior chamber.

243 Charles Street (14).

Miss Sylvia Landy and Mrs. Jane Towns gave technical assistance in these investigations. Dr. Frederic Merriam designed the micropipettes employed.

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Discussion

Dr. Wilhelm Buschke (New York): These studies by Dr. Kinsey are extremely interesting, and I would like to make a few comments in relation to the problem of still remaining possibilities for alternative explanations.

I would like to start with the last experiments, those on aphakic eyes. In the experiments which Mueller and I did some 15 years ago, we found low ascorbic-acid levels in aphakic eyes which were free from signs of irritation. Our experiments were done on rabbits' eyes which had been made aphakic many months and sometimes more than a year before the actual experiments were performed. In most cases several operations were necessary, because anybody who has tried to remove a rabbit's lens knows that it is practically impossible to do it intracapsularly without losing considerable amounts of vitreous.

I wonder if, in those cases in which Dr. Kinsey has found normal or even high levels of ascorbic acid after partial removal of the lens, the results could be explained by the presence of cortical and regenerating lens masses which may be particularly active in reducing ascorbic acid.

As a matter of fact, analyses of the glutathione content at various levels of the lens in the cortex and nucleus have shown that the concentration of this reducing substance is much higher in the cortex than in the nucleus, and I wonder if possibly a partial regeneration of lens masses could be responsible for maintaining ascorbic acid in a re-

duced state or for reducing dehydroascorbic acid, still holding on to possibilities of an explanation alternative to those advanced by Dr. Kinsey.

As a second comment, I should like to discuss the experiments with dehydroascorbic acid. I think one of the crucial points in these experiments is the concentration of the dehydroascorbic acid used as the starting level. I believe in the in vivo experiments that Dr. Kinsey did it was about 10 mg. percent.

DR. KINSEY: 100 mg. percent.

DR. BUSCHKE: That is about five times the concentration of ascorbic acid which is normal for the rabbits' aqueous. In some of the other experiments, that is, those in vitro, I think it was isotonic, on the order of 600 mg. percent, which is an order of magnitude quite different from the normal concentration of vitamin C in the aqueous. I wonder if the presence of such a large amount or concentration of dehydroascorbic acid could overwhelm the reducing system, in the sense that if there is a steady state between reduction and oxidation, due to the presence of a very large quantity of dehydroascorbic acid, the oxidation potential in the fluid would be raised to a level to create conditions unfavorable for the maintenance of any appreciable amount of reduced ascorbic acid.

DR. JONAS S. FRIEDENWALD (Baltimore): As Dr. Kinsey indicated, I have had the privilege of discussing this problem with him over the course of several years as he has developed his very meticulous efforts to try to find a crucial experiment with which to test the hypothesis, and to decide whether ascorbic acid enters the posterior chamber in the oxidized or reduced form.

While there is a paradox about the level of ascorbic acid in the aqueous in aphakic eyes, and the uncertainties of that experimental procedure are still unresolved, I do think that Dr. Kinsey has laid some very important ghosts in this whole series of experiments.

In the first place, I believe he adds final and definitive evidence against the hypothesis that has been urged by Fischer, that ascorbic acid in the aqueous is synthesized by the lens. His experiments now show that when the lens and aqueous are put together in the test tube, ascorbic acid does not rise in concentration but falls in concentration, and, if anything, the lens consumes ascorbic acid. That conclusion is supported by the in vivo experiments of finding a higher concentration of reduced ascorbic acid in the posterior than in the anterior chamber.

That one long-persisting hypothesis now, I think, has received its final demise.

As to the final question of whether ascorbic acid enters the aqueous in the reduced or oxidized state, its seems to me that the weight of evidence Dr. Kinsey has brought in is very persuasive. One can find some special hypothesis by which to cast doubts on each of these experiments, but for each experiment one needs a special hypothesis, and when you put all of these hypotheses together they don't make any reasonable summation.

I believe, therefore, the theory that Dr. Buschke and I advanced some years ago, that ascorbic acid reaches the posterior chamber in the oxidized form, may be also at least tentatively disposed of by the present experiments.

The basis for that theory, incidentally, was certain phenomena which we found in the ciliary body, which are still valid and which still suggest that ascorbic acid may be transported across the secretory boundary in the ciliary body in the oxidized form, as Dr. Kinsey has suggested; but the main reason why we thought it appeared in the posterior chamber in the oxidized form was the finding of the low level of reduced ascorbic acid in the aqueous in aphakia. Since those findings are now open to question, I think we have no positive reason for arguing against Dr. Kinsey's conclusions.

DR. V. EVERETT KINSEY (Boston): I would like first to thank the discussers of this paper, and to agree with Dr. Buschke

that I would place very little weight on our aphakic experiments. They were not satisfactory, and it is possible that the presence of the lens may act in some manner other than through direct reduction.

The question of whether we used too much dehydroascorbic acid I think is a well-taken possible objection. Our reason for using the quantity of dehydroascorbic acid we did was to shift the equilibrium in such a way that the lens had every opportunity to reduce ascorbic acid if it were going to do so.

However, as Dr. Buschke suggests, we may have so raised the oxidation potential of the system that reduction no longer could proceed. The only defense I have against this objection is that when crushed lenses were used reduction did take place. Nevertheless, in this instance more glutathione may have been present so that the oxidation reduction potential was not increased to the same extent.

With respect to Dr. Friedenwald's discussion, I agree that one can cast considerable doubt on any one of the experiments. However, if all the experiments are considered, one obtains the definite impression, I think, that ascorbic acid does not enter the eye as dehydroascorbic acid. The final word regarding this problem has not been given, and I would like to do some further experiments if I can plan a more crucial test. I hope others do likewise.

Perhaps at the next meeting of the association, the situation will be analogous to that which occurred when Dr. Hastings, professor of biochemistry at Harvard, was giving a talk on the synthesis of glycogen by the liver. He reminded the audience that he had spoken on the same subject three years ago, and that the last sentence of his lecture had been at that time, "Gentlemen, we can now say definitely that the liver does not synthesize glycogen from glucose. Tonight I can say that the liver does definitely synthesize glycogen from glucose."

Such is the progress of science.

THE CYANIDE SENSITIVITY AND CYTOCHROME-C CONTENT OF THE CRYSTALLINE LENS*

LAWRENCE O. ELY, M.D., AND W. A. ROBBIE, PH.D.
Iowa City, Iowa

The crystalline lens has an oxygen uptake which can be measured consistently in spite of the low rate of oxygen consumption of this tissue.[1] The QO_2† values of bovine, rabbit, and cat lenses are all approximately 0.09. The low level of metabolism which this represents may be visualized by comparing it with the following data on rat tissues:[2]

Temp.	*Tissue*	QO_2
370°C.	Kidney	21.0
	Brain	14.0
	Liver	9.0
	Large intestine	3.0

Both cytochrome and cytochrome oxidase are said to be absent from the lens.[3] However, Herrmann and Moses were able to prepare a system from fresh bovine lenses which would oxidize hydroquinone more rapidly in the presence of cytochrome C than without it, and they suggest that cytochrome oxidase is present in the lens.[4] This oxygen consumption was inhibited by cyanide. Because of this lack of agreement additional studies of the enzyme systems involved in the oxygen uptake of the crystalline lens are indicated, and the present paper reports a further study of the role of heavy metals in lens metabolism.

METHODS

Lenses from freshly killed young rabbits were used in the first part of this study. Extreme care was taken to obtain the lens intact.[1] Oxygen consumption was determined by the Warburg technique, using Ringer's solution, to which was added 200 mg. percent of glucose. The water bath temperature was 37°C. The cyanide concentration in the manometric experiments was controlled by using $Ca(OH)_2$-$Ca(CN)_2$ mixtures on the filter paper in the side arms.[5] Flasks having no center wells were used so that the capsules of the lenses would not be ruptured while the oxygen consumption was being measured.

Each of the investigators in this study worked independently of the other. One (L. O. E.) used rabbits weighing 3 to 4¼ pounds, with lenses of 91 to 131 mg. dry weight. The other (W. A. R.) used rabbits whose weight ranged from 2¼ to 3¾ pounds, with lenses of 58 to 114 mg. dry weight. The standard cyanide solutions were prepared separately. Results were tabulated together because there was no significant difference in the findings.

A quantitative spectrophotometric determination was made to see whether cytochrome C could be found in the lens, using a modification of the methods of Rosenthal and Drabkin,[6] and Potter and DuBois.[7] Five lenses were used in each preparation. Both bovine and rabbit lenses from freshly killed animals were analyzed. The lenses were homogenized with a glass Potter-Elvehjem homogenizer within a short time after the animals were killed. If homogenization could not be performed immediately, the intact eyes were kept in the refrigerator at approximately 4°C. until used. The homogenate was mixed with 0.25 ml. of distilled water, 1.25 ml. of 0.5M. H_2SO_4, and 0.5 ml. of 2 M. NH_4OH per gm. of homogenate, making a total volume approximately three times the weight of the lenses.

The precipitate was removed by centrifugation at 3,800 revolutions per minute for

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† Whenever used in this paper, QO_2 will mean the cubic millimeters of oxygen consumed per milligram dry weight of tissue per hour.

15 minutes. The volume of precipitate and supernatant were recorded. In the final calculations it is assumed that the cytochrome C is distributed equally between these two components.

The hemoglobin was removed and the cytochrome C precipitated by the method described by Rosenthal and Drabkin.[6] Final precipitation of the cytochrome C was facilitated sometimes by the addition of a small amount of purified protein to the preparation.

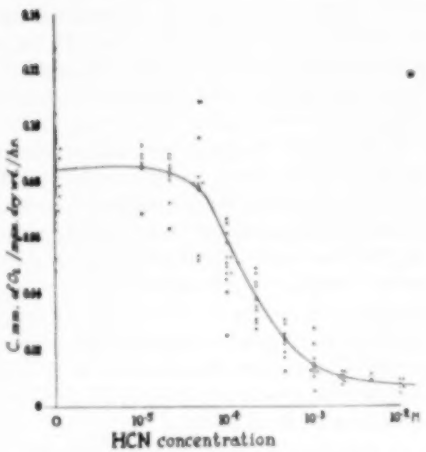

Fig. 1 (Ely and Robbie). Cyanide sensitivity of the respiration of rabbit lenses. The QO_2's (c. mm. of oxygen consumed per mg. of dry weight of tissue per hour) are plotted on the ordinate, and the molar concentration of hydrocyanic acid is represented by the abscissa.

The cytochrome C was analyzed in a Beckman Model DU spectrophotometer as ferrocytochrome C. The cuvette of this model holds a total of 3 ml. for analysis. The precipitated cytochrome C was brought into solution by adding distilled water to the final precipitate, bringing the total volume to 1 ml. To this solution was added 1 ml. of a phosphate buffer, pH 7.35,[8] 1 ml. distilled water, and a few crystals of sodium hydrosulfite ($Na_2S_2O_4$) in order to convert the cytochrome into ferrocytochrome C. This gave a total volume of 3 ml. of solution to be analyzed.

Recovery procedures showed that this method would measure amounts of cytochrome C in excess of 20 gammas per gm.

The final solutions obtained by the above methods are not of sufficient purity to disregard correction for contaminants. However, the method of calculation described by Rosenthal and Drabkin[6] can be used to compensate for these impurities. When the corrected optical density is obtained, the concentration in moles per ml. can be calculated from:[9]

$$C = \frac{D^{\lambda 550}}{\alpha},$$

where α is the absorption coefficient of purified ferrocytochrome C at 550 mμ, and equals 2.81 (cm.²/mole) × 10^{-7}.

The concentration per ml. is then adjusted for the total volume of solution and is changed to γ/gm. of tissue being analyzed (molecular weight of cytochrome C being taken as 13,000). A final correction is now made for the cytochrome C lost in the original precipitation during the first step of separating the cytochrome C for analysis.

Results

Figure 1 represents a compilation of the results obtained on cyanide sensitivity of the respiration of 120 rabbit lenses. The oxygen consumption is represented by the ordinate, and the cyanide concentration by the abscissa. The mean QO_2 of the 34 control lenses was 0.085. It may be noted that cyanide has little effect on oxygen uptake until a concentration of 10^{-4} M. HCN is reached. At this concentration approximately 50-percent inhibition is obtained.

About nine percent of the respiration is resistant to concentrations of cynanide as great as 10^{-2} M.

It is of interest to note the number of molecules of enzyme inhibited by one molecule of cyanide. Cyanide combines with cytochrome C when the iron is in the ferric state.

If one plots the log of the ratio of the inhibited respiration to the residual respiration against the log of the cyanide concentration, a linear curve results, whose slope is 1 (fig. 2). One can conclude from this result that

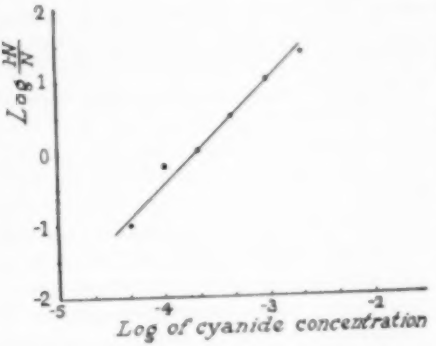

Fig. 2 (Ely and Robbie). Log of the ratio of inhibited respiration to residual respiration plotted against the log of cyanide concentration. Sample calculation: Let the maximal respiration equal 1, and the respiration at any cyanide concentration be N. Then the inhibited respiration is equal to 1 — N. At a cyanide concentration of 1×10^{-4} M. the mean respiration was 0.051. The maximal respiration was 0.085, and the cyanide-resistant respiration 0.007. Therefore, the cyanide-sensitive respiration is represented by 0.085 — 0.007, or 0.078. Correcting the value of mean respiration at 1×10^{-4} M. one gets 0.051 — 0.007, or 0.044. In terms of maximal respiration, 1, this value equals 0.044/0.078, or 0.564 which is N. 1 — N equals 1.000 — 0.564, or 0.436.

$$\log \frac{1-N}{N} = \log \frac{0.436}{0.564} = \log 0.773 = \bar{1}.888$$

one molecule of the active enzyme is inhibited by one molecule of cyanide.[2]

Repeated efforts were made to isolate cytochrome C from the lens. A total of 30 rabbit lenses and 65 bovine lenses were analyzed in groups of five by the method outlined. In no case was any cytochrome C found. This negative result indicates either that cytochrome C is absent from the lens, that it is present in quantities less than 20 gammas per gm., or that it is not freed from the cells by this method of preparation.

Discussion

It appears as if the oxygen uptake of the crystalline lens is dependent for the most part upon an enzyme which can be inhibited by cyanide. Cyanide is known to inhibit respiration by uniting with heavy metals which are an integral part of the enzyme system.

The work of Herrmann and Moses[4] with cytochrome C and hydroquinone indicates that cytochrome oxidase may be present in the lens. However, contaminants in the cytochrome-C preparation may cause interference in the cytochrome oxidase assay, and it is not clear from the published data whether this factor was adequately controlled.

There is present in the lens an appreciable content of copper.[3] Since cyanide combines with copper as well as iron, further investigation is indicated to determine whether a copper-carrying enzyme system may participate in the oxygen uptake of the lens.

Conclusions

1. The respiration of the crystalline lens of rabbits is inhibited by cyanide.

2. 10^{-4} M. HCN inhibits approximately 50 percent of the oxygen uptake.

3. About nine percent of the respiration of rabbit lenses is resistant to 10^{-2} M. HCN.

4. One mole of cyanide inhibits one mole of the active heavy metal-containing enzyme of the crystalline lens.

5. Quantitative spectrophotometric analysis indicates either that cytochrome C is absent from rabbit and bovine lenses, that it is present in quantities less than 20 gammas per gm., or that it is not separated from the cells by the methods used.

University Hospitals.

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Discussion

Dr. Jonas S. Friedenwald (Baltimore): I would like merely to answer the question raised about the work of Herrmann and Moses, which was done in our laboratory at the Wilmer Institute.

The cytochrome-C preparations which they had did not produce any oxygen uptake with hydroquinone in the absence of tissue extracts containing active enzymes. Controls on that were quite abundant.

Some oxidizer of cytochrome in the lens was indicated by their experiments.

Dr. Dische: I think this interesting experiment could perhaps be also interpreted in the following way, the outer layers of the lens, apparently, are the only ones that respire, because if you put the whole lens with the capsule into the ringer, the inner layer has no access to the oxygen. This, though, seems to be the physiologic conditions under which you are working.

Now, it could be that only the outer layer contains cytochrome C, and only the outer layer uses this system. Under these conditions the content of cytochrome C would be very low as calculated for the whole lens, and for this reason perhaps you could not find it.

Dr. L. O. Ely (Iowa City, Iowa): I am happy that Dr. Friedenwald pointed out this control by Herrmann and Moses. They did not publish a hydroquinone-cytochrome-C control.

Dr. Dische has correctly pointed out that the oxygen uptake of the lens is confined principally to the outer layers of the cortex. Quantitative spectrophotometric studies of cytochrome C show that liver has a cytochrome C content of 100 to 200 gammas per gm. The QO_2 of liver is approximately 8, or 90 to 100 times as great as the lenticular QO_2. Assuming that all oxygen uptake is through the cytochrome-C system in both liver and lens, and that all of the cytochrome C is active, one can calculate that the lens would contain about 1 to 2 gammas of cytochrome C per gm.

Further work is now indicated to clarify whether the oxygen uptake of the lens is mediated through a copper- or an iron-carrying enzyme system. One can go about this indirectly using inhibition of the oxygen consumption with carbon monoxide. Carbon monoxide unites with both iron and copper, inhibiting respiration of the tissue, the same as does cyanide. However, there is one distinctive difference: Light will reverse the oxygen inhibition in the iron system and will not reverse the inhibition of a copper-containing enzyme system. Preliminary studies by Dr. Robbie indicate that carbon monoxide inhibition of lenticular respiration is light-reversible. This finding suggests that the oxygen uptake of the lens is through an iron-containing enzyme system.

AUREOMYCIN IN OPHTHALMOLOGY*

JOHN G. BELLOWS, M.D.,** VIOLA M. RICHARDSON, M.D.,
AND CHESTER J. FARMER, PH.D.†
Chicago, Illinois

Aureomycin is an antibiotic obtained by Duggar[1] from a recently named mold, Streptomyces aureofaciens. This antibiotic is effective against numerous Gram-negative and Gram-positive organisms, as well as against some viral and rickettsial infections. Recently, Braley and Sanders[2] reported this agent to be effective in a variety of ocular infections caused by many infectious agents. The above findings, coupled with the high potency and low toxicity of this agent, indicated that aureomycin was potentially an important chemotherapeutic agent for ocular infections and warranted further investigations. A prime requisite for effective chemotherapy is that an adequate concentration of the antibiotic reach the infected site. We, therefore, undertook investigation of the penetration and distribution of aureomycin into the ocular tissues and fluids when administered locally and systemically. We also investigated the local tissue tolerance of aureomycin and the effect of this agent in some types of experimental and clinical ocular infections.

LOCAL EFFECT OF AUREOMYCIN ON OCULAR TISSUES

SURFACE EFFECTS

The instillations of drops of either a 0.5 percent solution of aureomycin borate or 1.25 percent solution of aureomycin ethylene diamine at four-hour intervals caused no untoward reaction in the rabbit or human eye. When the instillations were given at more frequent intervals, however—namely, 15 to 30 minutes as in two patients with hyperacute conjunctivitis—small corneal defects were noted within 24 hours upon staining with fluorescein. These lesions, because of their occurrence in the lower third of the cornea, suggested aureomycin as the cause.

Further evidence that aureomycin in the recommended concentration may injure the cornea was the observation that, when this antibiotic was applied to the rabbit eye by means of a corneal bath for 30 minutes or longer, faint, yellowish, abraded areas were occasionally produced. Powdered aureomycin borate, when placed in the normal rabbit eye, caused marked chemosis and staining of the palpebral conjunctivas and nictitating membrane with almost complete abrasion of the corneal epithelium after a 30-minute period. Aureomycin ethylene diamine in ointment form was found to be very irritating both to the rabbit and human eye.

EFFECTS ON CORNEAL REGENERATION

In order to observe further the local effects of aureomycin on the corneal epithelium, the effect of the antibiotic on corneal regeneration was determined. It is well known that many chemotherapeutic preparations and the more common antiseptics not only delay reepithelization but may also produce permanent vascularization and scarring.

The corneal epithelium of both eyes of a series of 12 rabbits was abraded by a process previously described.[3] The first group of four rabbits received one drop of aureomycin borate in a concentration of 25 mg. per 5 ml. of distilled water in the left eye three times daily. A second group of four rabbits received similar treatment with a concentration of 25 mg. per 3 ml. of distilled water. The third group of four rabbits were treated with a concentration of 25 mg. per 1 ml. of

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** Department of Ophthalmology, Northwestern University Medical School.

† Department of Biochemistry, Northwestern University Medical School.

distilled water. This latter is a saturated solution. The right eyes in each of the above groups, serving as controls, received one drop of saline three times daily. The eyes were treated for six days and stained daily with fluorescein to ascertain the rate of regeneration.

Group I. On the fourth day of the experiment, in the first group, corneal regeneration was complete in all the saline control eyes. Three of the four aureomycin-treated corneas had completely regenerated. The fourth showed, at this time, a small staining area which finally disappeared on the eighth day.

Group II. On the fourth day of the experiment, corneal regeneration was complete in but one aureomycin-treated eye of this group and in none of the saline controls of this group. On the fifth day regeneration was complete in two more aureomycin-treated eyes and two control eyes. On the eighth day, complete recovery had occurred in all eyes except for one saline control eye which still showed a small epithelial defect. This eye was normal on the 10th day.

Group III. Two saline control corneas of this group were completely regenerated by the fifth day. On the sixth day one treated eye was completely healed. By the eighth day, regeneration was complete in all eyes except for one aureomycin-treated cornea, which finally healed on the 10th day.

From these observations, it was concluded that, when all groups were considered together, no permanent damage as evidenced by vascularization, scarring, or ultimate retardation of regeneration occurred as a result of administration of aureomycin.

Intraocular effects

Aureomycin hydrochloride and aureomycin borate were injected intravitreally in a series of 12 rabbits in dosages varying from 50 to 1000 µg. per 0.1 ml. Immediately following injection, the aureomycin deposit was apparent in the vitreous as a yellowish, circumscribed area. In nearly all instances, on the day following the intravitreous injection, an intense, generalized congestion of the bulbar conjunctiva was noted. The aqueous humor contained cells and the iris became congested. This inflammatory response subsided within a few days, at no time obscuring the vitreous. Daily observation demonstrated the gradual dissolution of the yellowish mass into coarse and fine vitreous opacities. In some cases opacities were visible two months following injection. There were several instances of damage to the posterior lens capsule, attributable to trauma.

In general, no marked differences were observed between the aureomycin borate and the aureomycin hydrochloride in spite of the differences in pH. The number of opacities appeared to vary with the dosages used, being minimal with the lowest dosage. Large dosages injected intravitreally (10,000 µg. or more) produced a permanent, dense, white, vitreous opacity with loss of the red reflex and a proportionately greater inflammatory reaction in the anterior segment.

Comment

From these experiments, we conclude that aureomycin borate in a concentration of 0.5 percent is well tolerated in the eye, when instilled at 3 to 4 hour intervals. When this same concentration is applied by means of corneal bath, however, or when drops are instilled very frequently, damage to the corneal epithelium is sometimes noted. Epithelial defects caused by too frequent instillation of this antibiotic will usually heal within 24 hours, provided the number of daily instillations is diminished. Thus, the appearance of minor epithelial damage is not an indication that therapy should be discontinued, but merely lessened in intensity. Aureomycin in the recommended dosages does not retard regeneration of the corneal epithelium.

Regarding the injection of aureomycin into the vitreous, it is our impression that aureomycin produces considerably more damage than does penicillin or streptomycin similarly injected. It is moderately more damaging than bacitracin.

Penetration of aureomycin applied locally

Ordinarily, it is preferable to treat ocular infections, wherever possible, by local rather than systemic means. Local therapy, if feasible, permits adequate concentrations of antibiotic with minimum expense and without the risks inherent in systemic administration. Since rational local therapy depends upon a knowledge of the penetrability of aureomycin, we undertook investigations to determine the amounts of aureomycin in the aqueous humor following instillations, corneal baths, ion-transfer, and subconjunctival injections.

Instillations

Two drops of aureomycin borate solution (0.5 percent) were instilled at 10-minute intervals for a period of one hour in both eyes of three rabbits. After careful washing of the eyes with saline, the aqueous was aspirated. This aqueous was then assayed for aureomycin by means of a serial dilution type assay, employing B. subtilis which was sensitive to approximately 0.04 μg. of aureomycin per ml. Aureomycin was not present in detectable amounts.

Corneal baths

Aureomycin borate in a concentration of 0.5 percent was applied as a corneal bath using plastic, corneal eyecups to the normal eyes of a series of six nembutalized rabbits for periods ranging from 30 to 60 minutes. A second group of six rabbits, in three of which the entire corneal epithelium was abraded and in the remaining three of which the epithelium was abraded approximately 50 percent, received similar corneal baths for a period of 30 minutes. A third group consisting of three rabbits received corneal baths containing 0.5 percent aureomycin-borate solution to which was added one drop of 0.5 percent aerosol O.T. per ml. Corneal baths were also applied to a fourth group of three rabbits with active vaccinia keratitis.

Aureomycin did not penetrate the intact cornea. Abrasion and infection of the cornea, as well as the addition of aerosol to the antibiotic solution, readily permitted the penetration of aureomycin (table 1).

TABLE 1

Penetration of aureomycin (5000 μg. per ml.) by various means of local application

Condition of Cornea	Method of Administration	Time	Average Values in μg./ml. aqueous
Intact	Instillation	Drops every 5 min. for 30 min.	0.0
Intact	Corneal bath	60 min.	0.0
Abraded 100%	Corneal bath	30 min.	24.0
Abraded 50%	Corneal bath	30 min.	3.1
Intact	Corneal bath with 0.5% aerosol (1 drop per ml.)	30 min.	6.2
Mild Keratitis	Corneal bath	30 min.	10.0
Severe Ulceration	Corneal bath	30 min.	80.0
Intact	Ion-transfer	5 min.	.08
Intact	Subconjunctival injection	30 min.	.08

Subconjunctival administration

The injection of 2,500 μg. per 0.5 ml. subconjunctivally was performed in a series of six rabbits. After 30 minutes the aqueous was aspirated and assayed as previously described. Barely detectable amounts of aureomycin were found in the aqueous after repeated trial (table 1).

Ion-transfer

For the administration of the drug by means of ion-transfer, a Selinger iontophoresis apparatus was utilized. Approxi-

mately 2.5 ml. of a solution of aureomycin borate in the recommended concentration (5000 μg. per ml.) was placed in the eyecup, and anode transfer at a current of two milliamperes was carried out for a five-minute period. The aqueous was then aspirated and assayed as above. Following ion-transfer, corneal epithelial defects were noted which were of greater degree than those following lengthy corneal baths. However, after repeated trial, penetration of aureomycin was only of the order of that obtained with subconjunctival injection (table 1).

Comment

Aureomycin, like other antibiotics, does not penetrate the normal cornea in appreciable amounts. What is important, however, from the clinical standpoint, is that aureomycin does penetrate the abraded and inflamed cornea. Penetration with complete abrasion is appreciably higher than with 50 percent abrasion.

Likewise, severe corneal infection permits a higher order of penetration than a lesser degree of keratitis, probably due to marked thinning of the corneal tissues caused by ulceration. One drop of 0.5-percent aerosol solution per ml. of aureomycin ophthalmic preparation (0.5-percent aureomycin borate) results in moderate penetration through the normal cornea. With ion-transfer and subconjunctival injection, the amounts of aureomycin present in the aqueous were barely within the range of detectability.

Penetration and distribution of aureomycin in the ocular tissues and ocular fluids following systemic administration

Because of the limited supply of aureomycin available for parenteral use at the time of investigation, studies regarding the assay of ocular tissues for aureomycin were confined to determination of the results produced by intravenous administration. Aureomycin hydrochloride in a dosage of 50 mg. dissolved in 10 ml. of normal saline was administered intravenously to each of a series of three rabbits weighing approximately 1.5 Kg. each. After a 30-minute interval the eyes were enucleated and treated prior to assay as indicated in a previous publication.[4] Average values of the results stated in μg. per gm. of tissue or per ml. of fluid are given in Table 2.

TABLE 2

Average amounts of aureomycin in the rabbit eye

Serial dilution method with Bacillus subtilis	
Conjunctiva	6.0
Cornea	1.3
Sclera	1.5
Chorioretinal tissues	2.2
Vitreous	0.2
Aqueous	0.6

Comment

Aureomycin was found in the conjunctiva, chorioretinal tissue, sclera, cornea, aqueous, and vitreous in concentrations decreasing in the order named. As might be expected, the more vascular the tissue, the higher the aureomycin concentration. In one animal in which the aureomycin blood level was determined, it was found to be over 50 mg. percent. This level is considerably higher than that reported when aureomycin was administered orally and/or intramuscularly. This high blood level probably accounts for the significant levels found in the ocular tissues. Aureomycin concentrations of this magnitude cannot be expected with the recommended methods of administration and the smaller clinical dosages.

Experimental infections of the cornea

This study was undertaken to determine the efficacy of aureomycin therapy in infections of the cornea produced by Staphylococcus aureus, Pseudomonas aeruginosa, and vaccinia virus.

Staphylococcus aureus infections

Nine rabbits were anesthetized with nembutal and each was inoculated in both eyes

with a dilution of an 18-hour Staphylococcus aureus culture by injecting the organism into the corneal stroma in sufficient quantity to produce a uniform, opaque area 4 mm. in diameter. The concentrations of organisms ranged from the undiluted broth to a 10^{-6} dilution of the broth.* The rabbits will hereafter be designated according to the dilution which they received. The right eye of each rabbit was treated with 3 to 4 drops of aureomycin borate at 30, 40, 50, 60, 70, and 80 minutes following inoculation, while the left eye received saline at corresponding times. The rabbits were observed daily for a period of three weeks. From our observations, the results fall into three groups.

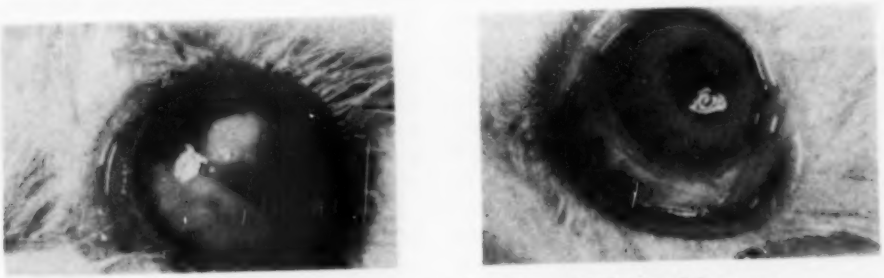

Fig. 1 (Bellows, Richardson, and Farmer). Staphylococcic infection of the cornea. (Left) Untreated eye. (Right) Eye treated with aureomycin.

The first group consisted of animals which received dilutions of organisms greater than 10^{-5}. With the exception of transient conjunctivitis or iris hyperemia in the control eyes, the response was essentially negative.

The second group comprised those rabbits receiving 10^{-5}, 10^{-4}, and 10^{-3} dilutions of organisms. Twenty-four hours following inoculation, the following conditions were noted in the control eyes: slight swelling of the lids, a generalized, mixed congestion of the conjunctival vessels, and a cloudiness of the central portion of the cornea. The anterior chamber showed a positive beam. The iris was congested. A day later, the diffuse cloudiness of the cornea developed into a grayish, white infiltrate. This finding was accompanied by a greater degree of conjunctival secretion and congestion, cloudiness of the anterior chamber, and muddiness of the iris. In two rabbits, the ulceration of the cornea resulted in dense, leukomatous scars. In the aureomycin-treated eyes, no infection was noted at any time (fig. 1).

In the third group of rabbits (those receiving 10^{-0}, 10^{-1} and 10^{-2} dilutions), evidence of serious infection was present within 24 hours, in the untreated eyes. There was marked swelling of the lids, secretion, intense engorgement of the conjunctival vessels, the formation of a corneal infiltrate, cloudiness of the anterior chamber, and congestion of the iris. By the third day, ulceration occurred with a marked degree of hypopyon. In 2 of the 3 rabbits, descemetoceles formed, followed by rupture of the cornea. In the treated eyes, the course of the infection was retarded, but infection was not prevented. Severe ulceration of the cornea occurred, but neither hypopyon nor rupture of the eyeball was ever observed.

Since the instillations of aureomycin were not effective in preventing infections in rabbits receiving the highest concentrations of organisms, more intensive treatment was then tried. A series of nine rabbits was inoculated with 10^{-0}, 10^{-1}, and 10^{-2} dilutions. Two corneal baths of aureomycin were given

* A plate inoculated with 1 cc. of a 10^{-4} dilution contained 2,000 colonies.

on successive days, treatment beginning immediately following inoculation. In addition, aureomycin ophthalmic preparation was instilled into the eyes three times daily. As a result of this more intensive therapy, infections, though not prevented, were of a milder degree. In one rabbit receiving a 10^{-3} dilution of the organism, infection was unusually mild, resulting in a nebulous scar.

It is apparent from the above experiments that complete prophylaxis resulted when aureomycin therapy was instituted immediately following inoculation with a moderate number of organisms (200 to 20,000 per ml.).

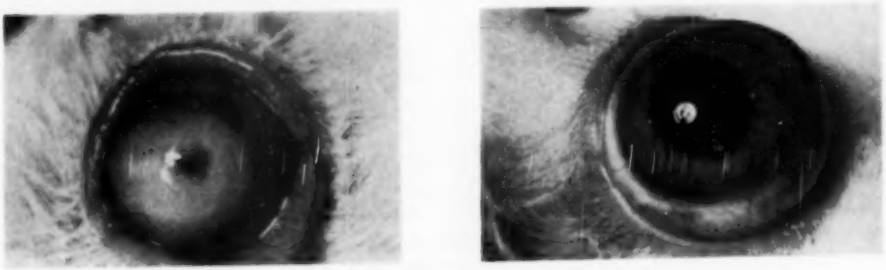

Fig. 2 (Bellows, Richardson, and Farmer). Pyocyaneous infection of the cornea. (Left) Untreated eye. (Right) Eye treated with aureomycin.

Investigations were undertaken to determine the maximum time interval which could elapse following inoculation, and yet give complete prophylaxis. A group of nine rabbits was used for corneal inoculation with a 10^{-4} dilution of Staphylococcus aureus. Treatment consisted in the instillation of several drops of aureomycin at three half-hour intervals and was instituted two hours, four hours, and six hours after inoculation. The untreated eyes became uniformly infected and appeared as previously described. The six rabbits which were treated within a four-hour interval did not develop infection. Infection did occur when treatment was delayed for six hours following inoculation.

Pyocyaneous infections

The corneas of 10 rabbits were delineated with a 4-mm. trephine, and the corneal epithelium within this area was denuded. A cotton tipped applicator previously immersed in a 24-hour broth culture of Pseudomonas aeruginosa was rubbed over the denuded area of the corneas for a period of one minute. Aureomycin therapy was started two hours following inoculation in three rabbits, four hours after inoculation in two rabbits, and six hours after inoculation in five rabbits. The concentration of aureomycin used was 10,000 µg. per ml., since in a previous experiment a concentration of 10,000 µg. per ml. of streptomycin was found to be effective in preventing infection when applied six hours following inoculation.[8]

Infection was completely prevented in the five animals treated within four hours after inoculation (fig. 2). Infection was prevented in one of the five animals treated six hours after inoculation, but all others showed corneal infiltration terminating in ulceration. The control eyes which were treated at corresponding intervals with saline showed severe corneal involvement leading frequently to the formation of descemetocele and rupture.

Vaccinia keratitis

The corneal epithelium of a series of eight rabbits was denuded in an area 4 mm. in diameter. Vaccinia was applied to the abraded cornea for a period of one minute,

during which time the lids were kept open. Immediately following, drops of aureomycin in the recommended concentration were instilled into the right eyes and this treatment was continued three times daily for seven days. The left eyes received saline simultaneously. Infections of equal intensity were noted bilaterally in all animals.

Comment

Aureomycin completely prevented experimentally produced Staphylococcic corneal infections provided the inoculum did not contain more than 20,000 organisms per ml. and treatment was instituted not later than four hours after inoculation. Aureomycin did not prevent infection when an overwhelming number of organisms was inoculated into the cornea.

The effectiveness of aureomycin against the ophthalmologically important, Gram-negative pathogen, Pseudomonas aeruginosa, was determined. This was done in spite of the fact that this organism has been shown to be only slightly susceptible to aureomycin. Growth of the strain used was inhibited by 100 μg. of aureomycin as demonstrated by the cup-plate method, but not by 50 μg. Infection produced by this strain was completely prevented when therapy was instituted within a four-hour interval.

Because aureomycin has been reported as effective against certain viruses including the herpetic and epidemic keratoconjunctivitis viruses, we investigated its effect against vaccinia. Aureomycin did not influence the course of experimentally-produced vaccinia keratitis.

Experimental vitreous infection

The purpose of this experiment was to determine the efficacy of aureomycin in experimentally produced Staphylococcus aureus infections of the vitreous. For this purpose the vitreous of both eyes of a series of 26 rabbits was inoculated with 0.1 ml. of an eight-hour broth culture of Staphylococcus aureus in various saline dilutions. Treatment consisted in the intravitreous injection of 0.1 ml. of saline containing varying amounts of aureomycin hydrochloride in the right eye, while the left eye of each animal, serving as control, received 0.1 ml. of saline intravitreously.

In order to determine the minimum concentration of aureomycin and the maximum time interval that may elapse for effective prophylaxis following inoculation, the following experiment was performed. In a series of 26 rabbits, inoculated intravitreally with approximately 100 organisms of this same culture, varying amounts of antibiotic ranging from 25 to 1000 μg. per 0.1 ml. were administered, either simultaneously or at 2, 4, 6, or 8 hours following inoculation. Results are shown in Table 3.

TABLE 3

The effect of intraocularly injected aureomycin in vitreous infection

No. of Rabbits	μg. of Aureomycin	Time	Results
2	25	Simultaneously	Panophthalmitis
2	50	2 hrs.	No infection. Few vitreous opacities
2	50	4 hrs.	Panophthalmitis
2	100	2, 4 hrs.	No infection. Few vitreous opacities
4*	250 & 500	2, 4 hrs.	No infection. Numerous vitreous opacities
8†	250 & 500	6, 8 hrs.	Vitreous cloudy. Red reflex absent
8‡			

* Two rabbits each were treated after two- and four-hour intervals.

† Two rabbits receiving 250 μg. were treated after a two-hour interval, and two rabbits receiving the same amount were treated after a four-hour interval. Two rabbits receiving 500 μg. were treated after a two-hour interval, and two rabbits receiving the same amount were treated after a four-hour interval.

‡ Interpret as above.

COMMENT

Aureomycin was effective against Staphylococcic infections of the vitreous when the proper concentration of the antibiotic was given within a limited time interval (fig. 3). Thus, 50 μg. of aureomycin prevented infection when administered after a two-hour interval, but not after four hours. At least 100 μg. was necessary to prevent infection after four hours. Between 250 and 500 μg., given after six- and eight-hour intervals, did not prevent infection, although infection was limited to the vitreous.

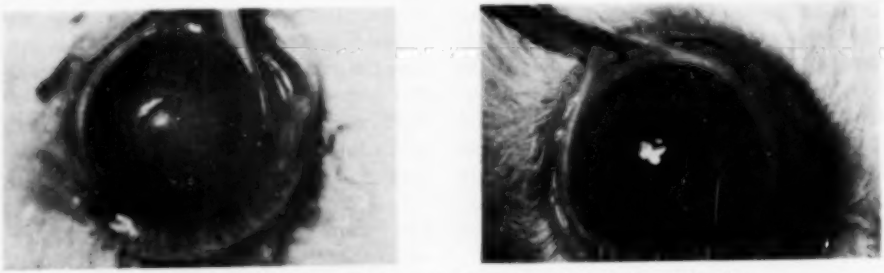

Fig. 3 (Bellows, Richardson, and Farmer). Staphylococcic infection of the vitreous. (Left) Untreated eye. (Right) Eye treated with aureomycin.

THE USE OF AUREOMYCIN IN CLINICAL OCULAR INFECTION

Following the favorable results obtained in the previously described experiments, aureomycin was administered to 41 patients, 38 of whom had external ocular infections, and three of whom had intraocular inflammation. External ocular infections were treated locally by the instillation of drops of aureomycin borate or aureomycin ethylene diamine in the recommended concentrations. The antibiotic was instilled at three-hour intervals in all patients with external infection, with the exception of three who had severe, acute epidemic keratoconjunctivitis and received instillations every 30 minutes for the first day of treatment. In cases of blepharitis, an aureomycin ointment preparation was used in addition to instillations.

The patients with intraocular inflammation received aureomycin hydrochloride by mouth in divided dosages totalling from 200 to 750 mg. daily.

In all cases of external infection, smears and cultures were obtained prior to therapy and the isolated organisms were tested for sensitivity to aureomycin, streptomycin, bacitracin, and penicillin. Aureomycin therapy was instituted immediately after the taking of the smears and culture and without knowledge of the bacteriologic and sensitivity findings. If, after 24 hours, the patient became worse or sensitivity tests revealed the causative organisms to be unsusceptible to aureomycin, this antibiotic was discontinued.

Treatment was, of course, continued in cases of epidemic keratoconjunctivitis in spite of negative bacteriologic findings as well as in one case of trachoma where inclusion bodies were demonstrable. Reports of patients, who were initially treated with aureomycin and who later were shown to have allergic reactions or irritations due to physical or chemical agents, were not included in this series.

STAPHYLOCOCCIC CONJUNCTIVITIS AND BLEPHARITIS

There were five cases of infections due to to Staphylococcus aureus. One patient with acute conjunctivitis recovered in three days. In a case of subacute conjunctivitis with corneal infiltrates, a dramatic improvement occurred within two days. Two cases of blepharitis were treated, one with no improvement, the other with moderate improvement

at the end of a week. The fifth patient, a child with severe, recurrent hordeola unsuccessfully treated with sulfonamides and penicillin for a period of many weeks, was completely recovered within five days.

Aureomycin therapy was instituted in nine patients with various eye infections, in whom the only organism which could be isolated was Staphylococcus albus. In four of these cases, an acute conjunctivitis completely disappeared in six days. In one case of anophthalmos with profuse discharge from the orbit, improvement occurred within four days with only a negligible amount of drainage remaining. A case of chronic conjunctivitis with corneal infiltrates improved after one week of therapy. Aureomycin was ineffective in three cases—a chronic blepharitis, a chronic conjunctivitis, and an acute conjunctivitis.

Mixed infections

There were seven patients classified as having mixed infections. In three, conjunctivitis was due to Streptococcus viridans and Staphylococcus albus. Improvement was noted in the two cases which were chronic, but no response occurred in the one which was acute. A fourth case of chronic conjunctivitis due to Pseudomonas aeruginosa and Staphylococcus albus likewise did not respond to aureomycin therapy. In a fifth case of chronic conjunctivitis, an unidentified Gram-negative rod and Staphylococcus albus were isolated. Improvement was noted in one week. Aureomycin was ineffective in the treatment of a sixth patient with acute conjunctivitis, from whose eyes Bacillis subtilis, Staphylococcus albus, and a diptheroid were cultivated. Hemolytic streptococci and Staphylococcus albus were isolated from a seventh patient with acute conjunctivitis and corneal infiltrates. The infection was completely cured after two days of treatment.

Hemophilis influenzae

In one patient with acute conjunctivitis due to Hemophilus influenzae, recovery was complete within three days at which time cultures were negative.

Pseudomonas aeruginosa

Two cases of acute conjunctivitis due to Pseudomonas aeruginosa alone were treated with aureomycin. In one case, accompanied by severe corneal involvement, the use of aureomycin in conjunction with delimiting keratotomy stopped the infectious process. Another case of conjunctivitis showed no improvement at the end of three days and could not be located for further follow-up.

Epidemic keratoconjunctivitis

Seven cases of epidemic keratoconjunctivitis were treated with aureomycin. Five of these were seen early in the acute phase. The sixth came under observation in a subacute stage showing many corneal opacities. The seventh was seen five weeks after the onset and had not responded to sulfonamides and other antibiotics. In two of the acute cases, an irregular denuded area was noted on the lower portion of the cornea 24 hours following the use of aureomycin at 15- to 30-minute intervals. Aureomycin therapy was continued at three-hour intervals, however, with subsequent healing of the cornea on the following day and recovery from the epidemic keratoconjunctivitis in a period of 7 or 8 days. In the remaining three acute cases, aureomycin therapy was started within 24 to 48 hours after the onset of symptoms, and recovery periods were 6, 7, and 10 days, respectively. In the subacute case, recovery occurred in one week's time. A dramatic response was noted in the seventh case 24 hours after the institution of treatment, and recovery was complete within four days.

Trachoma

In an acute exacerbation of trachoma of eight years' duration, in which inclusion bodies were demonstrated in the epithelial scrapings, marked subjective and objective improvement occurred after one week of local treatment.

Episcleritis

Two cases of episcleritis were treated with aureomycin, one locally and the other systemically. No improvement was noted in the patient who received local therapy. The patient treated systemically, however, completely recovered within two days. This patient received 50 mg. aureomycin four times daily by mouth.

Uveitis

Three cases of uveitis of undetermined origin were treated with atropine locally and by the oral administration of aureomycin. Recovery occurred within 24 hours in a case of acute iritis. A second case of iritis, first seen when the inflammation, although severe, showed signs of subsiding, completely recovered 48 hours after the institution of therapy. A third case of bilateral, chronic uveitis with frequent exacerbations was treated at the height of inflammation, in the left eye, with 250 mg. of aureomycin three times daily. No improvement was noted at the end of one week's time, and therapy was discontinued.

Comment

From the afore-mentioned clinical cases, it would appear that aureomycin is an effective agent in the treatment of certain Gram-positive, Gram-negative, and viral infections of the eye. It is impossible to draw definite conclusions from this series, because of the limited number of patients treated, but in general the results with staphylococcal, pneumococcal, streptococcal, and influenzal infections substantiate the favorable findings reported by Braley and Sanders.[2] In epidemic keratoconjunctivitis the period of morbidity was decreased to within 4 to 8 days. Beneficial results were obtained in one case of trachoma. The instances of successful treatment of uveitis described here and elsewhere,[2] coupled with the low toxicity and the present easy availability of aureomycin, suggest that the antibiotic merits further trial in this regard. Hypersensitization as a result of aureomycin therapy was never observed.

Summary

Aureomycin is well tolerated by the ocular tissues when the recommended dosages and methods of administration are employed. Aureomycin does not penetrate the normal cornea, but penetration through the inflamed or abraded cornea readily occurs. Following massive intravenous dosages significant amounts of aureomycin are found in the conjunctiva, chorioretinal layer, sclera, cornea, aqueous humor, and vitreous humor in amounts decreasing in the order named. Aureomycin is effective against staphylococcal infections of the cornea and vitreous. It is effective in corneal infections produced by a strain of Pseudomonas aeruginosa, but to a lesser extent than streptomycin. Vaccinia keratitis was not prevented by the use of aureomycin.

It is our opinion that aureomycin holds promise as being a useful addition to the therapeutic armamentarium of the ophthalmologist. It is the antibiotic of choice in certain viral diseases of the eye. It should be used in bacterial infections of the eye when sensitivity tests indicate the causative organism to have a greater susceptibility to aureomycin than to other chemotherapeutic agents. Although the reports of the value of aureomycin therapy in trachoma and uveitis are encouraging to date, further evaluation of additional cases is needed.

303 East Chicago Avenue (11).

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ENUCLEATION AND ALLIED PROCEDURES*

Part III. A new procedure involving use of an "exoplant"

Jack S. Guyton, M.D.
Baltimore, Maryland

The immediate or delayed insertion of an exoplant has been in use at the Wilmer Institute since July 15, 1946.

Development

About five years ago Dr. Conrad Berens remarked to me that the one way he could think of which should always prevent a buried implant from becoming displaced outside the muscle cone was to suture the rectus muscles together through tunnels in the implant. Application of this idea to an "exoplant," adapted for an attachable prosthesis, seemed logical because we had histologic evidence (fig. 13) that epithelium grew around and lined the smooth posterior portions of the original Ruedemann and Cutler implants.

It seemed likely epithelium would also grow around the muscles where they passed through smooth tunnels, provided the raw surfaces of the muscles were not pressed too tightly against the tunnels while epithelization was taking place, and such proved to be the case.

The term "exoplant" has been coined to denote that there is contact only with epithelized surfaces (once healing is complete) in contrast to the situation with semiburied implants.

The first exoplant† was inserted into a

† This first exoplant was made by Dr. Benjamin Poster (D.D.S.), who had experience in making plastic artificial eyes while he was in the Army, and who was both willing and able to translate sketches into plastic and metal reality. Dr. Poster was appointed prosthetist in the Wilmer Institute, a position he retained until recently (April 3, 1948), when pressure of his dental practice forced him to resign. He constructed all of the exoplants we used until February, 1948. Production was then undertaken by the Co-operative Dental Laboratories, 12 West Madison Street, Baltimore 1, Maryland. Prior to his recent resignation, Dr. Poster made the attachable prostheses for use with all the exoplants we inserted.

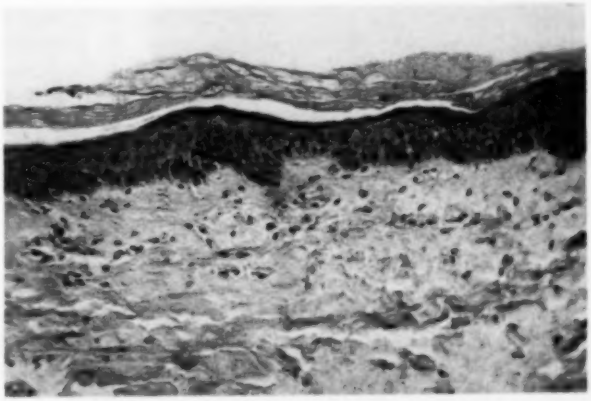


Fig. 13 (Guyton). Photomicrograph of the lining around the posterior pole of a Ruedemann implant, showing epithelium.

* From the Wilmer Ophthalmological Institute of The Johns Hopkins University and Hospital. Candidate's thesis for membership in the American Ophthalmological Society, accepted by the Committee on Theses.

socket where a Ruedemann eye had been extruded. By good fortune, this exoplant was sufficiently correct in size and shape that an excellent cosmetic appearance resulted which has persisted for 20 months. After a few exoplants had been inserted it became evident that the exoplant transmitted good motility to the prosthesis. As more and more late extrusions of ring implants were observed, while no late extrusions of exoplants occurred, the insertion of exoplants gradually became the procedure of choice for use after enucleation as well as for secondary or delayed insertion.

A great many sizes and shapes of exoplants were tried with about equal success if they were not too large. Four of the early exoplants inserted as secondary procedures were so large the muscles had to be sutured under tension; three of these were extruded within a few days after operation, and the other was retained but was later removed because it did not allow sufficient room for a proper prosthesis. Thereafter, smaller exoplants were used for secondary procedures, and no further difficulty due to size has been encountered.

At first, no attempt was made to hold the face of the exoplant in its proper position but, after three of the small size exoplants were found tilted (on the day after operation) so that prostheses could not be attached without operative correction of the tilt, various techniques were introduced for initial orientation.

Description of exoplant

The exoplant which is available at the present time is in the shape of a truncated cone on a hemispherical base. Two oval holes or tunnels pierce it perpendicular to its vertical (anteroposterior) axis and at right angles to each other, and the implant has a cup inset in its anterior surface (fig. 14).

Fig. 14 (Guyton). The exoplant and attachable prosthesis.

It is made in two sizes: the large size is designed for insertion at the time of enucleation and the small size is for delayed implantation or reimplantation. In both sizes the anterior surface is 12 mm. in diameter; the cup is 5 mm. in diameter at its opening, 4.5 mm. in diameter at its bottom, and 4 mm. deep, with a small flange inside the cup along its inferior wall; the distance from the anterior surface to the oval tunnels is 5.5 mm.; and the tunnels themselves are 4.5 mm. in vertical diameter and 5.5 mm. in horizontal diameter. In the large size the maximum diameter of the base is 18 mm. and the height of the base is 10 mm., giving an overall height of 20 mm. The weight is 3.5 gm. In the small size the maximum diameter of the base is 15 mm. and the height of the base is 7 mm., giving an overall height of 17 mm. The weight is 2.0 gm. All edges are rounded off and all surfaces highly polished.

The exoplants available at present are composed of methyl methacrylate, inset with a vitallium cup. Construction of these exoplants is as follows:[209]

A wax form is cast and lathed to exact dimensions. A hole is also lathed in the anterior surface of the form and the vitallium female cup is waxed in place. The wax form is invested in an injection-type dental flask and a mold of dental stone is made. The wax is eliminated by boiling it out, the mold is tinfoiled, and methyl methacrylate (approximately three parts polymer to one part monomer, varying slightly according to the weather) is injected into the closed flask with maintenance of a pressure of 400 pounds per square inch.

This assembly is placed in a Thermal Plasticure, to cure the acrylic, for six hours at a temperature of 170°F., and it is then cooled overnight. Tunnels are drilled through the exoplant, edges are rounded off, and all surfaces are pumiced and shined with polishing compound. Particular care is given to polishing the tunnels. All surfaces of the exoplant are examined under magnification to check against any porosity, roughness, or unpolished areas.

The female cup and the male pin (fig. 15) are cast of vitallium, which is an alloy containing 53-percent cobalt, 37-percent chromium and 10-percent molybdenum. The cups and pins are sandblasted, so they fit together perfectly, but they are not polished, because perfectly fitting polished surfaces tend to stick together.

Construction of all-vitallium exoplants, highly polished except inside the cup, and hollowed so as to weigh only 3 to 5 gm., is feasible but production (requiring expensive dies) will not be started until more time has permitted a better evaluation of exoplants as compared to semiburied implants, and has permitted any desired changes in size and design. Vitallium exoplants are theoretically preferable because this alloy assures permanency. Acrylic will probably also prove to be essentially permanent in its lasting qualities; however, acrylic plastic has only been in general use about 10 years, and it may deteriorate after much longer periods of time; a hypersensitivity to acrylic also occasionally develops.

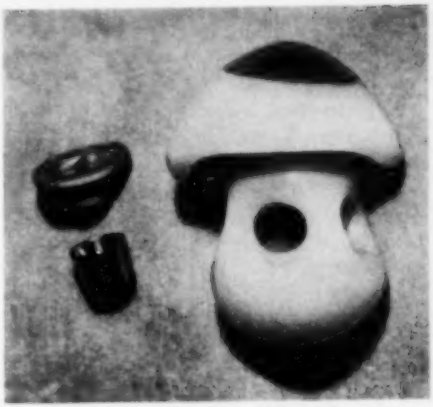


Fig. 15 (Guyton). Attachment of prosthesis to exoplant, and illustration of separate cup and pin.

Friedenwald[210] suggested that the exoplant might be sutured in place more easily if it were constructed in two parts with the junction passing through the tunnels, so that the anterior part could be screwed to the posterior part after the muscles were united. Iliff[211] has recently inserted two exoplants modified in this manner (fig. 16).

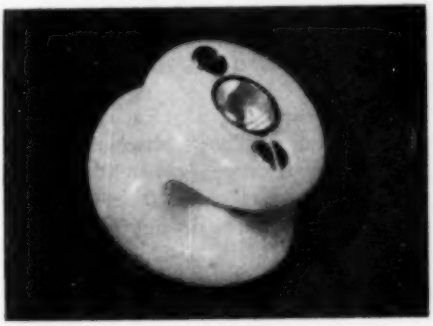


Fig. 16 (Guyton). Two-piece exoplant (Friedenwald and Iliff).

Operative techniques

A. Insertion of an exoplant at the time of enucleation

A pericorneal incision is made through conjunctiva, Tenon's capsule is separated from the globe, and each rectus muscle insertion is exposed, without disturbing its capsule. A double-ended 5-0 braided nylon

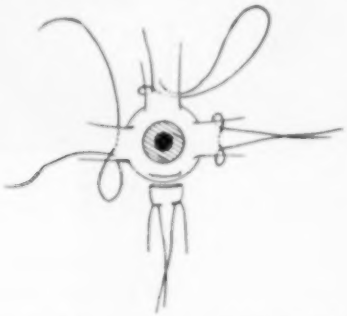


Fig. 17 (Guyton). Insertion of 5-0 braided nylon sutures to form a double-lock stitch in each rectus tendon.

suture, threaded and locked on ski needles 20 mm. in length, is inserted through each rectus tendon and capsule about 2 mm. from its insertion in such a manner as to form a double-lock stitch (fig. 17). Each rectus tendon is then divided at its attachment to the globe. The optic nerve is cut and the oblique muscle tendons are cut at their insertions, care being taken not to damage Tenon's capsule.

It is not imperative to wait until bleeding has completely subsided before inserting the exoplant, because blood can seep out around it for a short time postoperatively, but the bleeding certainly should not be brisk.

Both ends of the suture attached to the superior rectus are passed through one of the tunnels of the exoplant. Tenon's capsule is divided for several mm. back along each side of the muscle, just enough to permit the end of the superior rectus to be pulled completely through the tunnel and sutured to the inferior rectus tendon by means of the previously placed sutures, so that the tendons overlap each other 4 or 5 mm. Both ends of the suture attached to the internal rectus are then passed through the remaining tunnel of the exoplant, passing over the united vertical recti, and the end of the internal rectus is drawn completely through this second tunnel and sutured to the end of the external rectus (fig. 18).

The exoplant is now straightened into such a position that the anterior face tilts upward 15 to 20 degrees from the horizontal. This slight upward tilt allows for the slight downward rotation which will result from supporting the weight of the final prosthesis and the upper lid. The edge of the conjunctiva and anterior termination of Tenon's capsule are now tacked to each rectus muscle by means of a 5-0 plain catgut suture. These sutures are so placed as to hold the exoplant

Fig. 18 (Guyton). Uniting the muscles through the exoplant.

in proper position, by causing conjunctiva and Tenon's capsule to press snugly enough against the pillars separating the tunnel openings to prevent tilting out of position before the muscles adhere. A plastic conformer, with a large central opening (fig. 19A) to permit free drainage of any serous or mucoid discharge or of postoperative bleeding around the sides of the exoplant, is placed in the socket to maintain the conjunctiva in proper position in the fornices. A monocular

dressing is applied without pressure.

The above technique is that now in use. Actually, the exact details are of little consequence so long as the muscles are united firmly, without being under tension, and the exoplant is properly positioned.

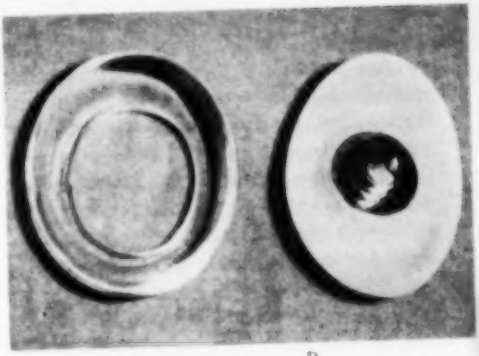
Different suture materials for uniting the muscle ends have included 4-0 mild chromicized catgut, and 6-0 to 3-0 silk, but 5-0 braided nylon appears preferable because it is amazingly strong for its size, causes a minimum of tissue reaction, and is easily handled. One precaution must be taken in using braided nylon: three ties are necessary, because a simple square knot may slip if the suture ends are cut off short. Any type of needle which can pass through the tunnels of the exoplant is suitable, but ski needles are the easiest to handle.

Fixation of the exoplant in proper position may be assisted by use of a conformer which has a pin projecting from its posterior surface, preferably 2 to 3 mm. above its center, to fit into the cup of the exoplant (fig. 19B). However, if the pin is so short as to allow the posterior surface of the conformer to rest against the face of the exoplant, there may at times be enough postoperative edema of the conjunctiva to push the conformer forward and disengage the pin. This complication can be minimized by using a very thin conformer with a longer pin.

A third method which assists in fixing the exoplant in position is to suture the junctures of the vertical and horizontal recti together. Such a suture is easily enough inserted, but is probably of little value unless the face of the exoplant has a tendency to tilt away from the desired position.

B. Insertion of Secondary Exoplants

Insertion of an exoplant into a socket where enucleation has previously been performed is dependent upon identification and isolation of the rectus muscles. The socket should be carefully inspected before operation, with the patient looking in the various directions, to determine the points in the



A B

Fig. 19 (Guyton). (A) Acrylic conformer with large central opening. (B) Conformer with pin, which can be used to fix exoplant in position.

socket where each rectus muscle exerts its maximum pull on the overlying conjunctiva. This is important even if general anesthesia is not used, because proper local anesthesia with novocain injection must produce partial or complete paralysis of the rectus muscles if pain is to be completely eliminated.

Toothed forceps are used to grasp an appreciable amount of firm subconjunctival tissue at each of the points where maximum pull on the overlying conjunctiva was exerted, and a stay suture is placed in each of these positions. With tension on the stay sutures, the rectus muscles can usually be actually palpated with a finger before the conjunctiva is incised (fig. 20).

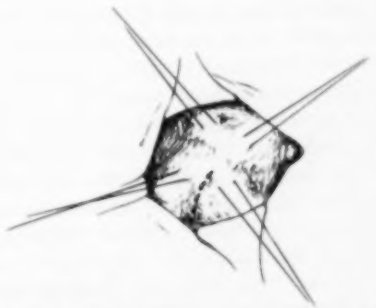


Fig. 20 (Guyton). Stay sutures and initial incision for delayed or secondary insertion of exoplant.

Identification of the muscles is by no means easy. After fibrosis around the muscles has taken place, there is little difference in appearance between muscles and fibrous tissue. The superior oblique is generally rather firmly attached to the superior rectus; this can cause confusion unless such an attachment is anticipated. The inferior oblique is likewise usually rather firmly attached to the inferior rectus, but this is less likely to be confusing.

In cases in which no previous implantation has been done there is usually a minimum of scarring to contend with, but considerable care must be taken in separating the recti from each other. Incisions are made between each pair of rectus muscles. Conjunctiva and fibrous tissue are dissected from over the muscles and each muscle is freed and cleaned so that it possesses moderate elasticity when stretched. Identification and isolation of the muscles is accomplished most easily by approaching each muscle from outside the muscle cone and exposing its external surface before a portion of the fibrous tissue is dissected from its sides and inside surfaces.

In cases of buried implants, the implants are invariably surrounded by a tough fibrous capsule which is quite difficult to separate from the surrounding orbital tissue. If the buried implant is definitely located in the center of the muscle cone, the capsule surrounding it can be excised and the rectus muscles identified and freed by approaching the inner surface of each. However, if there is any doubt as to the exact orientation of the buried implant, the recti are best identified by approaching their external surfaces.

Identification of the recti after extrusion of a semiburied implant is relatively easy, because each rectus muscle has generally been fixed by fibrous tissue in a readily accessible and identifiable position before extrusion of the implant.

Once the four recti are identified and freed, the exoplant is inserted in exactly the same manner as at the time of primary enucleation. If the socket is partially contracted, it is undesirable to suture conjunctiva to the recti. Introduction of an attachable conformer of large enough size will result in restoration of a proper socket when epithelization is completed, as well as in maintaining correct position of the exoplant.

C. Postoperative care

The monocular dressing is changed each day. If any appreciable discharge accumulates in the socket, it is cleaned by irrigation. Should any evidence of impending infection appear, antibiotics are used. Otherwise, the patient is allowed complete freedom.

Complete epithelization around the muscles and behind the exoplant apparently occurs within 2 or 3 weeks after operation. A conformer is worn for 3 to 4 months after operation, at the end of which time an attachable prosthesis is made for the patient. During the first two weeks the conformer with a central opening, permitting free drainage, may be used as long as position of the exoplant is approximately correct; a conformer with pin is then preferable to maintain proper position while contracture of the scar tissue takes place. After the patient obtains his prosthesis, he usually should remove it once or twice a day for irrigation of the socket.

Results

A total of 45 exoplants were inserted at the Wilmer Institute between July 15, 1946, and April 1, 1948. Twenty-five of these were inserted immediately following enucleation and 20 were placed in previously enucleated sockets. Seven were inserted following extrusions of Cutler ring implants, four after extrusions of Ruedemann whole eye implants, one after extrusion of a secondary exoplant, five in sockets with displaced buried implants, and three in sockets where no implantation had been performed. The follow-up records of these 45 cases cover periods varying from one week to 21 months, the average follow-up being six months.

The complications encountered with exo-

plants during the early development phase have already been enumerated as: (1) Three immediate extrusions, and one removal, of secondary exoplants which were too large, and (2) immediate tilting, sufficient to require operative correction, of four exoplants which were not fixed in position. Only one complication has occurred with the exoplants and techniques now in use. This consisted of extrusion of a secondary exoplant because of an acute pyogenic infection eight days after operation. Another exoplant was inserted successfully two months later.

In general, motility of the protheses was more uniformly perfect when insertion of the exoplant was an initial rather than a secondary procedure. Motility in the former instances was uniformly as full or almost as full as that of the normal eye, and approximately equal to that obtained with Cutler ring implants. Movement in the fields of action of the oblique muscles was as good as that in the fields of the recti, indicating that the oblique tendons were firmly attached to the subepithelial fibrous tissue surrounding the backs of the exoplants. Motility of the secondary exoplants was graded as perfect in eight cases, and cosmetically satisfactory but partially restricted in one or more meridians in the other eight. Deepening of the upper lid sulcus has been minimal in these cases, whether the exoplant was an immediate or a secondary procedure.

A theoretical objection to the exoplant is that, if the center of the base serves as the center of rotation, the radius of the arc in which the prothesis rotates will be 18 to 20 mm. The center of rotation of a normal eye lies 13.1 mm. behind the cornea when the eye is rotated downward, and 14.1 mm. when it is rotated upward; and the normal eyeball is itself displaced very slightly in the various meridians when it is rotated.[213-215]

At the time the first exoplants were inserted, the prostheses were constructed in much the shape of ordinary reform eyes. The prostheses therefore usually had a scleral curvature flatter than that of the normal eye, the average radius of scleral curvature being 14 mm. in the vertical meridian and 18 mm. in the horizontal meridian, and the prostheses were large enough to extend into the fornices. Motility of these protheses was somewhat limited because the edges of the prostheses were unable to rotate farther posteriorly than the fornices themselves would permit. After Dr. Cutler suggested that the prostheses should have the same curvature (both corneal and scleral) as the anterior portion of a normal eye, the original ones were replaced and motility was thereby considerably enhanced.

The prosthesis found best for use with exoplants (or with semiburied implants) usually has a scleral radius of curvature of 12.5 mm.

Jardon[216] describes a method for fixing a plastic pin onto stock Monoplex prostheses for attachment to semiburied implants. The Monoplex eyes were designed primarily for use as unattached protheses and are made in nine different sizes and shapes. The radius of curvature of the scleral portions of these eyes is variable in each model, being different in various meridians and at different distances from the corneal segment, with the curvature in the horizontal meridians averaging about 2 mm. more than the radius of curvature in the vertical meridians. Of the nine available sizes and shapes, model No. 3 most closely approximates the optimum shape of custom-made attachable prostheses.

The No. 3 Monoplex eye has scleral curvatures of about 13 mm. radius vertically and 14 mm. radius horizontally.[217] The over-all dimensions of this model exceed those optimal for attachable prostheses, but the edges can be ground down and repolished as desired. Jardon[218] believes a satisfactory attachable prosthesis can always be made from one or another of the stock Monoplex models. If such proves the case, the cost of the custom-made prostheses will be largely eliminated.

Summary

Ruedemann's introduction of semiburied plastic eye implants (1945), and Cutler's use

of a separate prosthetic section attachable by a male-female joint, initiated techniques which often result in a normal appearance and motility of artificial eyes.

The use of an "exoplant" which has contact only with epithelium, introduces a principle that may reduce the occurrence of late complications. The insertion of 45 exoplants (25 as initial and 20 as secondary procedures) at the Wilmer Institute during the past 21 months has given cosmetic results equal to those obtained with any of the semiburied implants and, as yet, there have been minimal complications.

The Johns Hopkins Hospital (5).

ADDENDUM. (January 3, 1950.) After this thesis was submitted (April, 1948), certain late complications began to appear in some of the cases in which exoplants had been used. During the 21 months since then, the following complications have been encountered:

1. In a moderate number of patients, the exoplant has gradually tilted away from the optimal position for support of and movement of the prosthesis. Such tilting has usually been downward, with stretching of the superior rectus where it enters the tunnel. It has occurred most often in those cases in which exoplants were inserted at the time of enucleation, especially when prostheses were obtained rather soon after operation. It has been least frequent when exoplants were inserted as delayed procedures into sockets already containing firm fibrous tissue.

An attempt is now being made to eliminate late tilting by the use of a modified exoplant, with a flatter posterior segment and an anteroposterior tunnel through which the obliques are sutured to the ends of the recti. In this way, the inferior oblique is used to help support the weight of the prosthesis and upper lid.

Other modifications include a smaller anterior surface, smaller tunnels, use of a slotted rectangular pin, and use of polymer alone in preparing the plastic.

2. In an appreciable number of cases, there has been excessive conjunctival irritation and discharge. In several instances, this has been associated with some orbital edema, or even orbital cellulitis. Irrigation of the socket one or more times daily with aqueous zephiran (1:5,000) containing one-percent sodium chloride appears to minimize such complications.

3. In a few instances, actual extrusion or necessary removal of the exoplant has been the result of one of these complications.

After a number of late complications with exoplants had been encountered, some of the semiburied tantalum-mesh implants were tried. Again, a number of late complications were encountered; these included excessive conjunctival irritation and discharge, actual orbital cellulitis, progressive exposure of the mesh, with eventual displacement of the implant in several instances, and recurrent hypertrophy of granulation tissue anterior to the mesh.

A tabulation of the results obtained with various semiburied implants and exoplants at the Wilmer Institute and at the Illinois Eye and Ear Infirmary is being prepared for publication. At the present time, however, superiority for any one or the other procedure cannot be claimed.

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NOTES, CASES, INSTRUMENTS

ANTERIOR-SEGMENT PHOTOGRAPHY*

WITH THE NORDENSON RETINAL CAMERA

NICHOLAS DOUVAS, M.D.,
AND LEE ALLEN
Iowa City, Iowa

The Nordenson retinal camera may be used to photograph the lens (figs. 1 and 2), iris (fig. 3), and external eye (fig. 4), in color or black and white without supplementary equipment and with only simple readjustments from the settings used for fundus photography.

The patient is seated before the camera with his head in the headrest as for fundus photography. On one side of the long horizontal barrel of the camera, in the rotating disc containing five spherical lenses of various powers is found a −1.5-diopter lens. This lens is rotated into position in the optical system for photographing all the above-mentioned structures. After the illumination is adjusted as in fundus photography, the whole camera is shifted toward the patient until its ophthalmoscope lens is about 4 cm. from the eye. The light emerges from the ophthalmoscope lens in the form of a cone and, because the base of the cone has been brought close to the eye, a circular area about 28 mm. in diameter is illuminated.

Using a 4-mm. arc with 5 amperes of current, a shutter setting of "2" makes good exposures of the external eye and iris on indoor Kodachrome or Ektachrome film. A shutter setting of "1" has been used for lens photography. These exposures compare with a setting of "0" for fundus photographs on the same film.

The side-arm focusing device functions properly for the photography discussed here without any change for settings used for fundus photography, and assures perfect focus with faithful recording of fine detail. General form is seen with the dim illumination from the carbon arc through the focusing filter, but the intensity of this light is insufficient for critical focusing on the external eye, iris, and lens. A small flashlight

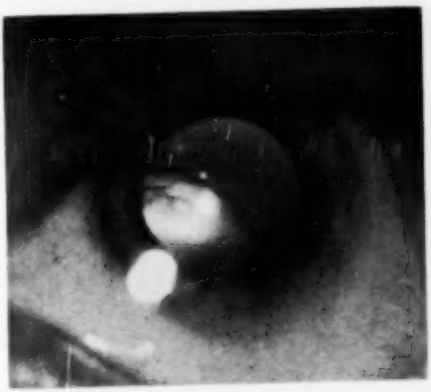

Fig. 1 (Douvas and Allen). Ectopia lentis, originally photographed with the Nordenson retinal camera on Ektachrome film, tungsten type; shutter setting, "1."

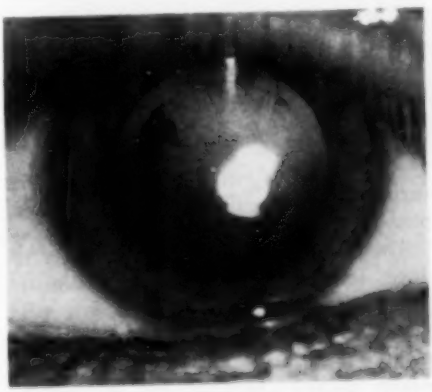

Fig. 2 (Douvas and Allen). Developmental cataract, perinuclear type, photographed with the Nordenson retinal camera on Eastman Plus-X film; shutter setting, "3."

* From the Department of Ophthalmology, College of Medicine, State University of Iowa.

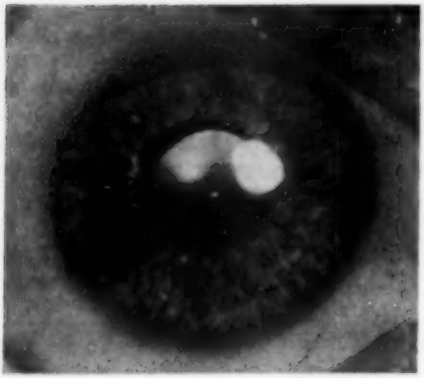

Fig. 3 (Douvas and Allen). Nevus of iris, originally photographed with the Nordenson retinal camera on Ektachrome film, tungsten type; shutter setting "2."

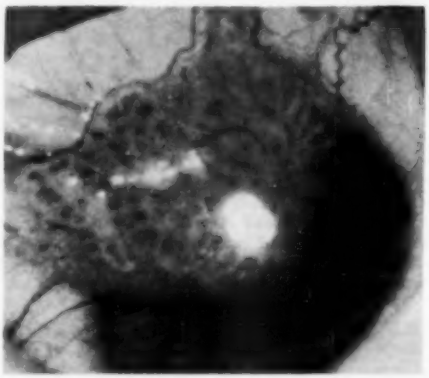

Fig. 4 (Douvas and Allen). Carcinoma of limbus, originally photographed with the Nordenson retinal camera on Ektachrome film, tungsten type; shutter setting, "2."

furnishes ample illumination for this purpose.

The focusing device reveals the light reflexes from the illuminating system in the position they will occupy on the photographic film. They may be shifted away from the point of greatest interest by moving the whole camera vertically or horizontally. These reflexes will move the same distance and direction as the camera. Smaller reflexes remaining upon and within the eye may be manipulated somewhat by having the patient shift his direction of gaze.

The image on the photographic film is approximately 1.3 times the size of the object, depending upon its depth within the eye. The pictures are 35 mm. in diameter with a circular outline. Most external pictures will have at least a small area of orange fundus reflex visible through the pupil.

Lens changes may be silhouetted against the bright orange reflex of the illuminated fundus (fig. 1) because of the co-axial nature of the illumination. The resulting picture is similar to the impression gained through ophthalmoscopic examination. This is one of the valuable uses of the camera.

Photographs of the iris made with the retinal camera often are superior to others because the reflexes can be placed over the pupillary area, thus leaving the entire iris visible.

Photographs of the external eye will be limited to a circular area, 25 mm. in diameter. The depth of focus in the Nordenson camera is more limited than in some others, but it is sufficient for showing the region of greatest interest.

University Hospitals.

DEVICE FOR STABILIZING THE ELECTRONIC TONOMETER DURING CALIBRATION

PAUL TOWER, M.D.
Los Angeles, California

The Mueller electronic tonometer represents a great improvement as compared to Schiøtz's mechanical tonometer. During calibration of the instrument, however, it is difficult to maintain the tonometer head in position, while at the same time adjusting both knobs. Thus, either the help of a second person is required, or the contact between tonometer head and test block has repeatedly to be interrupted and again established, making not only for loss of time but also for a

Fig. 1 (Tower). The wooden block with clip upright against the long side of the tray.

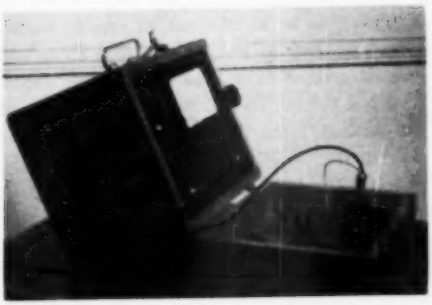

Fig. 2 (Tower). When the handle of the tonometer is inserted into the clip, the plunger remains in position over the test block.

Fig. 3 (Tower). The wooden block is folded down to the bottom of the tray.

certain amount of inaccuracy in readings and adjustments.

These shortcomings can be corrected by a single accessory designed to hold the tonometer head securely in place over the test block during calibration. A small, oblong wooden block with a slip at its upper end is placed against the long side of the tray formed by the lid of the instrument case (fig. 1). When the handle of the tonometer is inserted into this clip, (fig. 2) the plunger will be in a vertical position over the test block and will remain stable during the entire procedure. The little horseshoe-shaped wire attached to the collar of the plunger should never touch the base plate of the handle, as erroneous readings would result. The small wooden block is held in position by a hinge at the bottom of the tray, and is folded down before closing the case (fig. 3).

610 South Broadway (14).

INSTRUMENT FOR REMOVAL OF RUST RING OF CORNEA*

ERWIN E. GROSSMANN, M.D.
Milwaukee, Wisconsin

Harding† describes a simple instrument consisting of a stainless steel hypodermic needle mounted on a chrome-plated brass

* From the Department of Ophthalmology, Marquette University Medical School.

† Harding, G. F.: Arch. Ophth., **29**:134 (Jan.) 1943.

handle, which is useful in the removal of foreign bodies of the cornea. Appelbaum[1] simplified Harding's original instrument by attaching the same hypodermic needle to an ordinary insulin syringe. The use of a bevelled needle in the removal of foreign bodies from the cornea has been found satisfactory in most ophthalmologists' hands.

Although both Harding and Appelbaum state that the bevelled needle can also be used to remove a rust ring, it has been my experience that foreign bodies which strike the cornea and become impacted while hot, or

Fig. 1 (Grossmann). A dental burr inserted into an ordinary lead pencil is used for removal of rust rings of the cornea.

metallic foreign bodies that remain in the cornea a few days, or oxidized areas from a shower of sparks will nearly always leave a "rust ring" which is part and parcel of the continguous corneal tissue. This is especially true of emery foreign bodies which always strike the cornea in a heated condition.

Simple manipulation with a sharp-pointed instrument will not always remove the oxidized area without some degree of piece-meal extraction and a consequent insult to the corneal tissues. The obstinate "rust ring" usually requires removal by a fine corneal curette, or by twirling a dental burr between the thumb and forefinger.

The short dental burr is not easy to manipulate and has a tendency to shift slightly from the desired site. Cross, therefore, devised a "chuck," to which an ordinary dental burr can be attached, and this instrument has been used for years by industrial surgeons.

I have used a similar "chuck" for the past two years, made from an ordinary lead pencil, and have found this improvised instrument to be as efficient as one of metal. One-half inch of lead is removed from one end of an ordinary lead pencil. The shank of a No. 0.5 or No. 1.0 dental burr is dipped into ordinary mucilage and inserted into the hole in the pencil. After a few minutes, the shank is firmly glued into the handle (fig. 1).

Since dental burrs are not stainless or rust proof and cannot be boiled, it does not matter that the metallic instrument is mounted on a wooden shaft. To sterilize the dental burr is immersed in a bottle of 70-percent alcohol for 30 minutes, or for 10 minutes in any of the phenol preparations used for ophthalmic cutting instruments. The various-sized dental burrs can be used to suit the particular case. In all of my cases, a smooth clean crater has always been obtained.

238 West Wisconsin Avenue (3).

[1] Appelbaum, A.: Arch. Ophth., **30**:262 (Aug.) 1943.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

SECTION ON OPHTHALMOLOGY

February 17, 1949

DR. PERCE DELONG, *chairman*

SURGICAL TREATMENT OF GLAUCOMA

DR. JOHN H. DUNNINGTON, New York, the guest speaker, discussed the reasons for failure of primary surgical treatment for glaucoma, and offered some suggestions for the prevention of such failures and for secondary operations if required. He first pointed out that the two most common causes of failure are: (1) Faulty selection of surgical procedures, and (2) faulty technique.

Dr. Dunnington quoted the procedures of choice for various types of glaucoma as suggested at a symposium at a recent meeting of the American Academy of Ophthalmology and Otolaryngology. The reasons for their selection were outlined, and it was pointed out that paracentesis of the anterior chamber in acute narrow-angle glaucoma is inefficient, as is iridectomy in obstinate cases of this type.

He referred to Chandler's discussion of faulty technique, and stressed this as a very important preventive factor. The cases of operative failure were divided into two groups:

1. Those in which ocular tension remains high.

2. Those in which ocular tension subsequently rises.

In the first group fall most of the cases in which the original procedure was a poor choice, the best illustration being paracentesis for acute narrow-angle glaucoma, which calls for iridectomy or a filtering operation.

If the original operation was an iridectomy or filtering procedure, hemorrhage or a damaged lens may be the cause of failure. A swollen cataractous lens must be removed promptly. Hemorrhage is a very difficult problem and must be handled with great care. If absorption has not begun in 48 hours, a very careful corneal paracentesis is recommended.

For hemorrhage into the vitreous, spontaneous absorption is preferred. Posterior sclerotomy in the region of the ora serrata was mentioned and, if other procedures are unsuccessful, nonperforating cyclodiathermy is worthy of trial.

Most failures in glaucoma surgery fall into the second group. A careful survey to determine the cause of the secondary rise in tension was urged. If the cause is uevitis, either severe or quiet, the treatment should be the measures used in glaucoma secondary to uveitis, rather than re-operation. Spontaneous recovery in such cases is not infrequent, and Dr. Dunnington advised waiting at least two months for a secondary operation in such a case. Miotics and mydriatics are used with great care. Ten-percent neosynephrin to keep the iris mobile is often useful when miotics are used.

Granting that re-operation is indicated, the multiplicity of procedures available is evidence of their frequent inefficiency. If an iridectomy has been done and the iris is healthy, an iridencleisis is preferred in cases with tension not over 45 mm. Hg, and sclerectomy with iris inclusion in the more severe cases.

If the iris is atrophic, a trephining operation is preferred. If there are peripheral anterior synechias, the site of the trephining operation should be chosen where these adhesions are minimal. One trephination does not preclude another at a different point away from previously formed scars.

Cyclodialysis is usually not helpful in the presence of a narrow or obliterated angle. A combination of cyclodialysis and iridectomy was described for certain cases where another filtering operation is not considered feasible.

M. Luther Kauffman,
Clerk.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

February 7, 1949

Dr. Benjamin Esterman, *president*

Beta irradiation in keratitis

Dr. Clara L. Okrainetz discussed the value of beta irradiation in the treatment of corneal lesions. Since Beta rays are absorbed in the first 3 mm. of tissue, Beta radiation is an ideal approach to effective treatment of diseases of the cornea without causing cataract formation. The radium-D applicator used at the Manhattan Eye, Ear, and Throat Hospital was described.

Beta irradiation is known to be very effective in occluding corneal blood vessels and proved to be of great benefit in keratoplasties. Occasionally good results with partial clearing of the opacities are obtained. Also, if proper irradiation is used, good results are obtained in recent, as well as in chronic, corneal lesions with thickening and vascularization.

Two cases of chronic corneal ulcers successfully treated with Beta rays were presented by the Radiotherapy Department of the Manhattan Eye, Ear, and Throat Hospital.

The first case was that of a man, aged 31 years, with a corneal ulcer, of the left eye of three months' duration, resistant to systemic as well as local medication. With only three applications of Beta rays (1500 r. each) there was almost complete clearing of the cornea.

In the second case, a very good result with similar irradiation was also obtained. A woman, aged 62 years, had a dendritic ulcer of the cornea of five months' duration. Cauterization and systemic therapy gave no results.

The mode of action of Beta irradiation in keratitis in speculative. It has been pointed out that the Beta rays increase the antibody reaction in the cornea, and it may be that the beneficial result is obtained in this way. Or perhaps, the treatment at the limbus produces occlusion of the vessels and, with decrease in vascularity, improvement follows. Whatever the mode of action is, Beta irradiation should be given in every case of keratitis in which the more conservative methods have failed.

Discussion. Dr. Esterman asked if this method has any other advantage other than simplicity of application.

Dr. Okrainetz replied that this method produces more rapid results and fewer applications are required.

Hole in the macula

Dr. Abraham Kornzweig presented a paper on this subject. The complete report is on pages 243-247 of this issue.

Pigmentary retinal degeneration with external ophthalmoplegia

Dr. Max Chamlin presented a paper on the condition known as progressive nuclear ophthalmoplegia (or hereditary external ophthalmoplegia), which is believed to be a heredo-degenerative entity, and occurs alone or in combination with bulbar and spinal nuclear palsies. In 1944, Barnard and Scholz described cases of external ophthalmoplegia associated with pigmentary degeneration of the retina. Walsh describes three more of these cases.

Except for the pigmentary degeneration of the retina, these cases had practically the same features as the so-called progressive nuclear ophthalmoplegia. They all started in adolescence or early adult life and showed

external ophthalmoplegia. Ptosis was a prominent and early feature.

Dr. Chamlin presented three cases which fall into the same category.

The first case was that of a boy, aged 13 years, with a marked bilateral external ophthalmoplegia that had started with ptosis at the age of nine years. In addition he had pigmentary degeneration of the retina.

The second case was that of a girl, aged 14 years, who also had a bilateral external ophthalmoplegia with pigmentary degeneration of the retina. The ophthalmoplegia had started with ptosis at the age of 12 years. In addition, this patient showed optic neuritis.

The third case was that of a woman aged 26 years, with a bilateral external ophthalmoplegia that had started with ptosis at the age of 13 years. She also had early pigmentary degeneration of the retina and, in addition, some bulbar palsy.

All three of these cases fall into the same category of ophthalmoplegia with retinal degeneration as described by Barnard and Scholz and Walsh. In all three cases, the pigmentary changes were a little difficult to find but were definitely present. When found, it helped to place these cases into a heredodegenerative category and rule out myasthenia gravis, tumors, vascular malformation of the brain stem, and pathologic conditions at the apex of the orbit which might require angiography, X-ray air studies, or surgical intervention.

Sclero-tenonitis

Dr. Frederick H. Theodore presented a case of unilateral sclero-tenonitis in a man, aged 75 years, who first developed a localized anterior scleritis. Three days later intense chemosis occurred, with almost complete immobility of the eye, slight proptosis, and moderate pain. The tenonitis cleared up in 10 days with three injections of foreign protein.

Tenonitis is sometimes confused with orbital cellulitis. In tenonitis, however, the proptosis is slight and the chemosis is marked. In scleritis, the eyeball is not fixed. Epidemic keratoconjunctivitis should be differentiated by the prominence of the conjunctival symptoms and the preauricular lymphadenopathy. Trichiniasis may show a picture resembling tenonitis, with involvement of Tenon's capsule, and may arise secondary to myositis. Tumors of the orbit may simulate the picture, but inflammatory signs are not present.

Discussion. Dr. Adolph Posner asked Dr. Theodore if he thought that the foreign-protein therapy caused the recovery in this case, or was the disease self-limiting.

Dr. Benjamin Esterman asked which foreign protein was used.

Dr. Theodore replied that he did not know whether it was the foreign protein which caused the recovery. He said that he had given two typhoid injections and one injection of milk.

Acute iridocyclitis and chronic simple glaucoma

Dr. Victor Goodside said that coincidental association of acute iridocyclitis and chronic simple glaucoma is of rare occurrence. A 48-year-old woman was presented. She complained of pain and redness in the right eye of five weeks' duration. Questioning elicited the further complaint of recurrent transient appearance of colored halos about lights for a period of two years.

Ocular examination revealed typical findings of acute iridocyclitis in the right eye. The left eye was completely normal except as to tonometric examination. Intraocular pressure was: O.D., 22 mm. Hg (Schiøtz); O.S., 50 mm. Hg. Following cautious instillations of mild mydriatics in the right eye, therapy continued with instillation, three times daily, of atropine (one percent) in the right eye, and pilocarpine (three percent) three times daily in the left eye.

Tension in the left eye was rapidly normalized, and the acute iridocyclitis in the right eye subsided without rise in tension. Four days later, the pupil of the right eye

was widely dilated, the globe was white, and no evidence of the recent iritis could be observed except for a few pigment deposits on the anterior lens capsule. The left pupil was miotic. Intraocular pressure was: O.D., 28 mm. Hg (Schiøtz); O.S., 23 mm. Hg. Atropine was discontinued in the right eye; pilocarpine was continued in the left.

On August 27, 1948, 18 days from the date of first examination, the intraocular pressure was elevated for the first time: O.D., 35 mm. Hg; O.S., 20 mm. Hg. Pilocarpine was begun in the right eye and intraocular pressure two days later was: O.D., 27 mm. Hg; O.S., 20 mm. Hg. Tension has remained normal to the present time under miotic therapy in each eye.

Optic atrophy due to gunshot wound

Dr. Howard Weisberg presented a case of a white man, aged 32 years, who was admitted to the hospital on October 5, 1948, in a semicomatose conditon apparently the victim of a mugging attack. Examination revealed a deep laceration anterior to the right ear one inch in diameter and a large "puncture laceration" one and a half inches long in the face lateral to the right eye. The patient complained of not being able to see.

There was marked swelling of the right eye and a moderate degree of ecchymosis of the left eye. Both pupils were widely dilated and did not react to light or accommodation. The extraocular movements were limited in all directions on the right, due apparently to the extreme peribulbar swelling, but were normal on the left. The fundus picture of both eyes was entirely normal.

One week elapsed, during which time the patient complained of not being able to see even light. A spinal tap was done and revealed a grossly bloody fluid and a pressure of over 200 mm. of water. At this time he also exhibited a partial peripheral right seventh-nerve palsy with inability to close his lids. There was also a partial right ptosis and movements of the right eye downwards and in the field of motion of the right superior oblique were affected. Both pupils were still widely dilated, the right somewhat more than the left. Both were nonreactive to light and accommodation. The fundi still appeared normal.

X-ray films revealed a 0.38-caliber bullet lying behind the left eye. This bullet had entered in the right temporal region and passed behind the right eye to sever the optic nerve, and then entered the left orbit to do similar damage there. A second badly fragmented bullet was located in the right petrous bone.

On October 29th a craniotomy was performed using a transfrontal approach. After some manipulation the bullet was delivered intact. The patient was discharged from the hospital on November 15th, completely well but blind.

Phages and filtrates in lid infections

Dr. Daniel Kravitz reported the rapid and excellent results obtained in 116 unselected cases of eyelid infection treated with bacterial filtrates. Wider treatment with bacterial phages and filtrates is recommended to avoid unnecessary allergic reactions and complications from the use of penicillin and sulfa drugs, which can always be used if the phages and filtrates fail.

This paper was published in full in the Journal, Volume 32, page 1047, August, 1949.

Bernard Kronenberg,
Recording Secretary.

COLORADO OPHTHALMOLOGICAL SOCIETY

November 20, 1948

Dr. Ralph Danielson, *presiding*

Retrolental fibroplasia

Dr. Edward Swets presented a premature infant who was born at the Colorado

General Hospital on May 7, 1948. The expected date of confinement was August 5th. The birth weight was 2 pounds 11 ounces. The mother was gravida 10, para 10. The cause of prematurity was not evident. Laboratory studies of mother and infant were normal with respect to blood counts, R H factor and serology. While in the hospital the infant had frequent cyanosis, diarrhea, and pneumonia. A diagnosis of congenital heart disease was made. Before discharge, an eye examination revealed normal external findings and a good red reflex from each fundus.

On October 21, 1948, the child was examined in the eye clinic. There was no red reflex from the right eye, which had the appearance of a typical case of retrolental fibroplasia. A dim red reflex was obtained from the left eye. A retrolental mass was seen inferiorly in this eye. Examination under general anesthesia was not done because of the risk involved due to the congenital heart disease.

Discussion. Dr. Danielson stated that the eyes of all premature infants born at Colorado General Hospital are examined before they leave the hospital. So far 150 cases have been seen. Until the past three weeks no retrolental fibroplasia has been found. Two cases have been seen in the last three weeks. This condition was considered a congenital anomaly until the work of the Owens demonstrated that it developed after birth. Possibly a hemorrhage into the vitreous may be the cause.

Chorioretinitis

Dr. Edward Swets presented a white man, aged 30 years, with a tentative diagnosis of chorioretinitis juxtapapillaris of Jensen. The right eye had an irregularly defined gray-white lesion extending from the temporal edge of the optic disc to the macula. In the macular area were several small ill-defined lesions of the same type surrounding the large area. The left eye had a similar picture.

The patient had been discharged from the army in 1941 because of a chronic otitis media. At the time of discharge the eyes were apparently normal except for a slight horizontal nystagmus which the patient dated back to 15 years of age. During 1941, the vision of the right eye gradually decreased to 20/200. He had no treatment at that time. He was first seen by an ophthalmologist in May, 1948, when vision of the left eye began gradually to decrease.

In June, 1948, he was hospitalized for study. Vision of the left eye was 20/25 when the patient was first seen at the clinic. Soon after this a central scotoma of approximately 10 degrees appeared and the vision decreased to 20/200. An underlying vascular basis for the lesion of the left eye was present, the vessels in the central area of the retina being quite tortuous. Several small, deep choroidal hemorrhages appeared during the progress of the disease.

Tuberculin tests, blood sugar, Brucellergin, and Wassermann tests were negative. A medical examination was negative. Treatment had included courses of penicillin and sulfathiazole systemically, atropine solution locally, graduated injections of old tuberculin and typhoid vaccine intravenously. The condition had become stationary.

Discussion. Dr. Horton said that histamine given over a long period for vasodilatation helped in many cases of old choroidal lesions and retrobulbar neuritis. Dr. Kafka had had improvement in macular degeneration of arteriosclerotic origin with the use of Lilly's histamine acid phosphate given every other day, keeping under a reactive dose, for 15 to 20 injections. After four months, there is visual improvement. Dr. Droegemuller felt that dicumarol improves vision in some cases of retinal degeneration.

Use of contact lenses

Dr. Kaplan presented a 24-year-old man who had a trauma to the left eye four years ago causing the lens to become opaque. The lens had completely absorbed. In the past year he had been bothered by diplopia and

felt that the vision of the left eye was blurring that of the right. Uncorrected vision: R.E., 20/20; L.E., 10/400. In March, 1948, he was fitted with Feincone contact lenses with a resultant vision of 20/15 in each eye. These have been worn most of the time with comfort, although near vision has been difficult. The patient has good depth perception.

Discussion. Dr. Droegemuller said that he believes contact lenses have a place. Dr. Chapman mentioned a similar case in a 15-year-old boy. She had fitted contact lenses which brought the vision to normal. Testing him on the eikonometer, she found that, even with a 10-percent size correction, there was still so much difference in image size that he was unable to fuse the images of the two eyes.

Procedures with nevi

Dr. Kafka presented a white boy, aged 10 years, who was first seen on February 27, 1948. At that time a black speck was visible at the limbus of the left eye at the 3-o'clock position. The slitlamp revealed a nevus at the site and a second nevus about 3 mm. temporarily. The mother stated she had noticed a small black spot during the boy's infancy but thought it had disappeared. Periodic examinations were made and no change was noted until one week ago. Both nevi had increased considerably in size. The conjunctiva was elevated, melanotic in appearance, and had several feeder vessels.

Discussion. Dr. Nelson said that, if such a lesion grows, he performs a biopsy with the patient on the table and, if reported malignant, removes the lesion at once with diathermy.

Dr. Hopkins thought a biopsy alone would cause a spread of the lesion. Dr. Koplowitz said that such lesions are radio-resistant and radium treatment is contraindicated. Dr. Bane said that he follows these cases by photographing periodically so that he has a definite comparison.

Dr. Danielson advocated measurement of the lesion each month and removal if any growth were noted. Dr. Strong said he enucleates the eye if there is an increase in size of the lesion.

Dr. Filmer had had a 40-year-old patient with a pigmented lesion at the limbus and did an enucleation with excision of the conjunctiva. The pathologic report was metaplasia without malignancy. He felt enucleation was the correct procedure. Dr. Crisp favored the idea that this lesion was malignant because there were two areas.

Katharine Chapman,
Secretary.

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PROFESSOR HJALMAR AUGUST SCHIØTZ

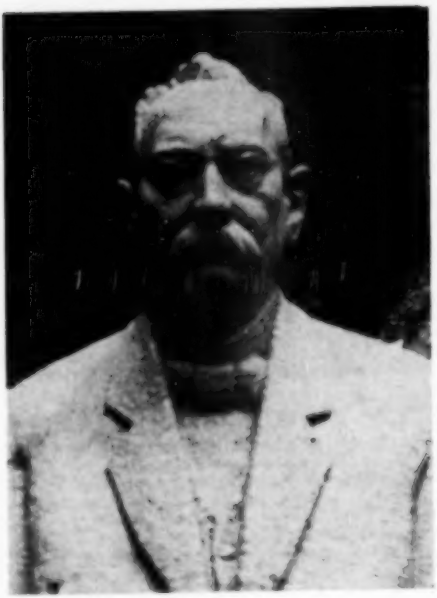
(February 9, 1850-December 8, 1927)

Information comes from our esteemed correspondent, G. W. Keyser of Oslo, Norway, that the ophthalmologists of Norway have subscribed to a bronze bust of Schiøtz as part of their centennial tribute to this celebrated teacher, investigator, and clinician. Dr. Keyser, one of the last and most devoted of the assistants of Schiøtz, has kindly submitted at our request the accompanying photograph of the bust by Carl E. Paulsen together with personal recollections of his great chief. The following sketch is based on this correspondence and various other sources.

Schiøtz was the first professor of ophthalmology in Norway. Before his appointment in 1901, the University Clinic included ophthalmology as a division of surgery. Thanks to the continued effort of Schiøtz a special clinic devoted wholly to ophthalmology was built in 1915.

Schiøtz was born in Stavanger on February 9, 1850, graduated as bachelor of medicine in 1877, and interned at the Rikshospital

(University Clinic) until 1879. Deciding to specialize in ophthalmology, he studied in Vienna under Ernst Fuchs and Arlt for six months, and for the next 15 months was associated with Javal in his Laboratory of Physiologic Optics at the Sorbonne. Javal referred to this coöperation as "the best days of my life." The ophthalmometer was first exhibited at the Milan Congress in 1880.



Bust of Schiøtz

Owing to the junior status of Schiøtz, the instrument was termed the Javal ophthalmometer until Javal corrected his confreres at a meeting in Lucerne in 1904: "They have not done justice to my collaborator, Dr. Schiøtz, who played a very important role in our work. The instrument should always be called the ophthalmometer of Javal and Schiøtz."

After his return to Norway in 1881, Schiøtz worked under Hjort in the surgical department of the Royal Hospital at Oslo as clinical chief of the Ophthalmic Service. Years later when a young ophthalmologist asked him to see a case of panophthalmitis following cataract extraction in a patient's single eye, Schiøtz responded sympathetically: "Call for me at any time. I know what Professor Hjort did for me when I was young."

His thesis, "On some optical corneal characteristics," completed in 1883, obtained for him the doctorate. Following the illness of Hjort, he became head of the government eye hospital in 1889.

The tonometer, on which he had worked three years, was demonstrated before the Norwegian Medical Society on May 12, 1905. His laboratory experiments were originally made on a small metal drum closed above by a thin rubber membrane, the drum being connected with a water manometer. Physical considerations showed that the plunger sinks into the membrane until the depressed area is supported from below by a pressure that balances the weight of the plunger. He continued his measurements and calibration with numerous human eyes in situ after death, using a cannula of one-mm. lumen in the anterior chamber.

Schiøtz also invented the first self-registering perimeter, a lantern for the examination of color vision, and an ophthalmoscope of his own design. He published several treatises in Norwegian, including textbooks for undergraduates that were translated into English, French, and German. For the invention of the tonometer the government honored him with the distinguished decoration, Commander of the First Class of the Order of St. Olav.

Schiøtz had a versatile mind with a pronounced technical and mathematical turn, and continued to the end of his days with the construction and improvement of instruments. He was a keen diagnostician, a skillful surgeon, and in his early years popularized the aseptic technique he had learned abroad. Nevertheless, he always had to master a profound depression on entering the operating arena. In temperament he was reserved, painstaking, considerate, amiable and

warm-hearted. His students nicknamed him "All-father," the name attached to Odin by their pagan ancestors.

Schiøtz held his professorship until the age of retirement, in 1922, but could not retire from his professional interests. In 1927, he devised the x-tonometer with the convex plunger, which like his original instrument gave a constant deflection but was safer for the corneal epithelium and more precise in borderline cases of increased intraocular pressure. A week before his fatal stroke he gave a demonstration in skiascopy before the Oslo Ophthalmological Society. After eight days of coma, he quietly passed away on December 8, 1927, at the age of 78 years.

James E. Lebensohn.

THE ACADEMY'S SYMPOSIA

For the last two years the American Academy of Ophthalmology and Otolaryngology has presented one or more symposia on pertinent subjects. These have all been excellent authoritative reviews and have been in great favor with the members.

The symposium, as given before many societies, usually consists in the presentation of a selected subject by a group which has been assigned to discuss its various phases. Frequently the men have not conferred so that there is an overlapping; in addition, there is often a divergence of opinion, leaving the listener more confused than ever.

There is nothing haphazard about a symposium as presented by the Academy. The subject is chosen two years in advance by the secretary of ophthalmology. The chairman is then selected by the secretary and he in turn selects the various subdivisions to be discussed. A team of authorities is then chosen and a subject assigned to each. Work on the symposium is started immediately. During this stage, there is a good deal of correspondence between the chairman, the secretary, and the members of the team.

One year preceding the meeting at which the symposium is to be presented the team has a long conference at which each member presents his material. This is discussed, overlapping is eliminated, and differences of opinion are ironed out. Here the final plans are made and the presentation planned.

In the spring preceding the presentation there is a "dress rehearsal" with the illustrations and the final material. This affords an opportunity for any minor changes that seem indicated. It also permits any change in the illustrations that may be suggested. Final meetings are then held a day or two preceding the actual presentation.

Thus the symposium represents the opinion of a team of authorities who have given the subject a coördinated study and consideration over a two-year period. Therefore, in place of confusing the issue, it presents the clearest possible picture of the subject as based on present-day available knowledge. Obviously, the passage of time and new discoveries will alter some of the opinions expressed.

The care given the presentation of these symposia is very evident and accounts for their having become one of the most popular features of the Academy's program.

The secretary of ophthalmology is to be congratulated upon his vision in making the symposium a means of presenting the best possible current opinion of the authorities on some phase of ophthalmology.

Frederick C. Cordes.

CORRESPONDENCE

CHARTING VISUAL FIELDS

Editor,

American Journal of Ophthalmology:

In the November, 1949, issue of the JOURNAL is a most interesting article by Zugsmith and Rehman concerning "A simple, more accurate means of charting visual fields."

I desire to congratulate the authors, but at the same time I should like to correct some of their statements.

The flash perimeter which I produced was not cumbersome and models have been in use

by Sir Purves Stewart of London, Dr. Hale Haven of Seattle, Dr. Loyal Davis of Chicago, and myself among others. At the Ophthalmic Section meeting of the A.M.A. in 1936, I demonstrated the neon flash perimeter and an article appears in the volume for that year. In the AMERICAN JOURNAL OF OPHTHALMOLOGY, **20**:828, 1937, I published an article on "Evolution of flash perimetry." My two handmade models are still in excellent working order. Instead of a hand wand I use an adaptor which rides the ordinary Schweigger hand perimeter.

All of my work was done at Northwestern University Medical School in Chicago, and V. Mueller of that city considered making the instrument, but Mr. Wallerick advised that perhaps Bausch and Lomb or American Optical would be in a better position to market my instrument. Keep up the good work.

(Signed) Leo L. Mayer,
St. Louis, Missouri.

DR. ZUGSMITH'S REPLY

Editor,
American Journal of Ophthalmology:

I regret the use of the word "cumbersome" in our article in the November, 1949, issue of the JOURNAL; certainly, I meant no slight on Dr. Mayer's work. His excellent and pioneer efforts in the field of flash perimetry should effect wider use of the instrument, which is surely more accurate and simpler than using test objects.

My feeling was that a small, portable instrument, which could also be used for tangent-screen work, would persuade more ophthalmologists to use this method.

Both Dr. Mayer and I are trying to change what amounts to a custom and I defer to any criticism that he may choose to make.

(Signed) George S. Zugsmith,
San Pedro, California.

A SIMPLE AID IN PRESCRIBING BIFOCALS

Editor,
American Journal of Ophthalmology:

While sitting in church recently, I noticed that the elderly gentleman with high myopia who sat in front of me had evidently refused bifocals. He was constantly attaching clip-ons to read the book he held in his hand and removing them to look at the minister in the pulpit. It occurred to me that he was no better off than he would have been with two pairs of glasses. However, if his clip-ons had been made in bifocals with a plano top, he would have had all the advantages of bifocals with fewer of their disadvantages.

Consequently, I have used this device in several instances with complete satisfaction to the patient and to me. Although it is possible that other ophthalmologists already use this aid, I have found no reference to it. I would, therefore, like to suggest it for general use.

(Signed) Morris Kaplan,
Denver, Colorado.

BOOK REVIEWS

THE EYE AND ITS DISEASES. Edited by Conrad Berens, M.D. Philadelphia and London, W. B. Saunders Company, 1949, second edition. Cloth binding, 1092 pages, 436 illustrations including eight in color. Price, $16.00.

The second edition of *The Eye and Its Diseases* adheres as closely as possible to the outline of the first edition. The number of writers has been increased to 92. Each contributor has revised his section of the book and several distinguished ophthalmologists have written new chapters or revised chapters appearing in the previous edition. There are additional chapters on illumination, physiologic chemistry, and on gonioscopy.

The general appearance of the book has been changed somewhat by double column printing; it is more pleasing in appearance

and easier to read. The recent advances in therapeutics have been considered and care has been shown in selecting material on antibiotics and new chemotherapeutic agents to be included in the book. Many of the contributors have brought their bibliographies up to date in keeping with the advances in ophthalmology.

This book has much to recommend it. Like all books written by more than one contributor there is a certain inherent disunity in style and presentation. Some of the chapters are too broad in their scope, the authors being forced to summarize and delete necessary material in order to accommodate the subject to the allotted space. This allows only an elementary study of some subjects and reduces the value of the text as a reference book. These criticisms are of minor importance, however, and the student, the practitioner, or the ophthalmologist who consults this book will find that it covers the essentials of ophthalmology and in many respects it is excellent.

Irving Puntenney.

PRACTICAL ORTHOPTICS IN THE TREATMENT OF SQUINT. By T. Keith Lyle and Sylvia Jackson. Philadelphia and Toronto, The Blakiston Company, 1949, third edition. 271 pages, 151 illustrations including three in color. Price, $8.50.

The original edition of this well-known book was published 12 years ago and was intended "to provide a practical manual for orthoptic students." Its scope has been broadened in the second and third editions so that it now provides good reference material for both the ophthalmologist and orthoptic technician. In this latest edition more emphasis has been placed on the theoretical, etiologic, diagnostic, and surgical aspects of squint.

Sylvia Jackson, one of the pioneers in the field of orthoptics, has contributed much to make the chapters on diagnosis and orthoptic treatment complete. Many advances have been made in the general treatment of strabismus since the last printing in 1940. During this period, Lyle has carried on extensive studies on muscle imbalance in the Royal Air Force. The long analytical tables formerly included in the text have been omitted and case histories, many from the files of the Royal Air Force, now serve as illustrative material.

As a result of this experience, Lyle has rewritten the chapter on "Heterophoria." His analysis and suggested therapy are well presented. Studies on pilots have contributed much to the sections on etiology and symptomatology. A fairly inclusive outline of examination is given in order to evaluate the binocular state in relation to the amount of latent deviation.

Chapter XVII, "Paralytic strabismus (acquired)," has also been rewritten and includes a thorough clinical analysis of diplopia fields and abnormal head postures resulting from paralyses, secondary contractures, overactions, and palsies of the extraocular muscles. Although clinically complete, little emphasis has been placed on the laws of innervation which are necessary for their proper understanding. Suggested surgical procedure is outlined for cases of individual muscle paralyses and local orbital injuries causing relative palsies. The role of orthoptics, before and after surgery, in the reestablishment of comfortable binocular vision is presented.

There is in England a uniquely satisfactory relationship between the ophthalmologist and orthoptist. Of value for the American reader is the text's clarification of the position of orthoptics in cases of muscle imbalance and defective fusion. It makes clear the type of case which is not orthoptic material and that which may be expected to benefit by orthoptic treatment, either alone or in conjunction with surgery.

Carolyn King.

MAY'S MANUAL OF DISEASES OF THE EYE. By Charles A. Perera, M.D. Baltimore, Williams & Wilkins Company, 1949. 20th edition. 512 pages, 378 illustrations, including 32 plates with 93 colored figures, index. Price, $5.00.

The old friend and companion to generations of medical students, practitioners, and ophthalmologists is back with us again in modern habiliment. Many of the familiar but antiquated illustrations have been replaced with new ones and several have been added. New material includes the treatment of conjunctivitis with penicillin, other molds and the sulfonamides; a working classification and description of diseases of the optic nerves; the use of newer biotics; toxoplasmosis; standard surgical operations; an excellent rewritten chapter on disturbances of motility of the eye; and a remarkably compact yet satisfactory chapter on the ocular manifestations of general disease.

Dr. Perera has been eminently successful in bringing this edition up to date with a skilful economy of words that permits him to retain the comfortable size of the book so familiar to us, at the same time including new material. This achievement resembles the miracle of the loaves and fishes.

Derrick Vail.

MICROPHTHALMOS AND ANOPHTHALMOS WITH OR WITHOUT COINCIDENT OLIGOPHRENIA. By Torsten Sjögren and Tage Larsson. Copenhagen, Norregade, 1949.

This work is a painstaking statistical and genetic analysis of microphthalmos and anophthalmos with or without coincident oligophrenia (feeblemindedness) occurring in Sweden. Since 1896, it has been obligatory in Sweden that all blind persons under 20 years of age be reported yearly to the Institute for the Blind. In subsequent years, more elaborate records and diagnoses have also been included. The result is a mass of material sufficient in quantity to calculate accurate statistics.

Microphthalmos or anophthalmos with oligophrenia appears to be inherited as partially sex-linked with a reduced degree of manifestation. Microphthalmos or anophthalmos without oligophrenia appears to be a dominant hereditary disease.

Among the interesting data brought to light is the fact that German measles in the mother during pregnancy could not possibly account for more than an occasional isolated case. Forty-four percent of the cases with oligophrenia had toxoplasma determinations and were all negative. Syphilis also was not a factor in the occurrence of these cases.

A great deal of time, effort, and thought must have been expended to turn out such an excellent, comprehensive, and scientific work.

Orville E. Gordon.

THE PHYSIOLOGY OF THOUGHT. By Harold Bailey, M.D., F.A.C.S. New York, The William-Frederick Press, 1949. 314 pages, clothbound. Price, $3.75.

The author, who is 76 years of age and has been in medical practice since 1897, is a life member of the American Academy of Ophthalmology and Otolaryngology. His analysis of the thought process is exemplified by the following excerpts:

"Even though the function of our senses is dependent on our consciousness, the knowledge that we are conscious depends upon our senses . . . the stimulus of a sense impression may arouse thought, but the recognition of the nature of the stimulus becomes possible only after thought has been aroused. . . . Our memories spell the difference between consciousness and intelligence. . . . When thought reaches a certain volume, we have knowledge that we are thinking and are therefore aware that we are conscious."

This nontechnical volume should be of interest to the many medical and lay friends of the author.

James E. Lebensohn.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

5

DIAGNOSIS AND THERAPY

Hesse, Erich. **Temporary total blepharoraphy in military injuries.** Klin. Monatsbl. f. Augenh. **115**:31-35, 1949.

Temporary blepharoraphy is indicated in lagophthalmus due to facial paresis, keratitis neuroparalytica, orbital injuries with protrusion of the bulbus, certain wounds of the lids and after certain plastic procedures. The author describes a method which avoids freshening up the lid margins. He puts the membrane of a fresh egg on cornea and sclera, then he runs two double armed sutures deep through the orbital muscles and includes a small roll of gauze in the stitch. One suture runs through the upper and lower lid on the nasal and one on the temporal side. The sutures are said to hold the lids together efficiently and have proven their value in six cases. (3 figures.)

Max Hirschfelder.

Kapuscinski, W. **Capsular lenticular lens extraction from the superior border.** Ann. d'ocul. **182**:757-760, Oct., 1949.

The author describes a new type of capsule forceps. The shank is angled backwards and the blades are reversed forming a V-like angle. The short arm is approximately 2 mm. long. With this forceps the capsule is grasped in reverse position as compared with other capsule forceps. The lens capsule is grasped near its upper margin with the short arm of the forceps and the lens is extracted. The force is directed downward, then anteriorly and then upward and anteriorly. The author has also used these forceps in the extraction of hypermature lenses, and after micropuncture.

Chas. A. Bahn.

Salvadori, Luciano. **Tissue therapy in ophthalmology.** Ann. di ottal. e clin. ocul. **75**:101-126, April, 1949.

Thirty-one patients with various ocular diseases were treated with subconjunctival implantations of placenta. From his study of these patients Salvadori inclines, with reservations, to a favorable opinion of Filatov's tissue therapy. He notes particularly that old corneal opacities unchanged for years may clear partially in a relatively short time. Less striking improvement was noted in the case of vitreous opacities, visual acuity and fields, and night blindness. Instead of autoclaving at 120° C. the tissue to be

transplanted, as Filatov recommends, Salvadori soaked it in a solution of penicillin, and although the active substances are thermostabile he believes that placental tissue thus treated may be more efficacious. Henry K. Messenger.

Woods, A. C. **Therapeutic action of streptomycin and promizole in clinical ocular tuberculosis: a preliminary report.** Arch. Ophth. **42**:521-537, Nov., 1949.

This article is the latest report (Academy, Oct., 1949) by the author on his epoch-making researches in tuberculosis. There were two guiding principles in the choice of patients to be treated. The first principle was that the diagnosis of ocular tuberculosis in any treated patient must be so firm that it would meet the approval of an experienced ophthalmologist. The diagnostic criteria observed were as follows. The ocular disease must conform to a pattern commonly regarded as tuberculous, and one in which histologic examination of eyes with similar disease patterns had uniformly demonstrated the probable tuberculous nature of the disease. The patient must show elsewhere in the body evidences of a preceding tuberculous infection, a source from which the ocular infection might logically have arisen. The cutaneous reactions to tuberculin must be in conformity with those for the patient's age and tuberculous status. The most thorough and exhaustive medical survey possible should reveal no other systemic disease or cause to which the ocular inflammation could logically be attributed. The details of this diagnostic survey have been outlined elsewhere. The second guiding principle in the selection of patients was that the ocular disease either had not yielded to more conventional forms of therapy or did not appear amenable to such therapy and that the condition of the patient was sufficiently desperate to warrant any risk that this treatment might entail.

The author's conclusions are: 1. streptomycin given in doses of 0.5 gm. twice daily, combined with promizole in the amount of 6 gm. a day in divided doses had a dramatic effect in controlling the clinical evidence of activity and inflammation in the 14 patients with frank ocular tuberculosis so treated; 2. a therapeutic response was observed after 9 to 21 days of treatment. The response thereafter was slow but steady; 3. irreversible changes, such as corneal scarring, cataracts, vitreous opacities and organic tissue damage, were not influenced by such treatment and reversible changes, that is, corneal infiltrates, nodules in the iris, choroidal exudates and all inflammatory changes regressed; 4. toxic symptoms appeared in a large percentage of patients so treated. These symptoms were not serious and, if the drugs were discontinued, promptly disappeared without residue; 5. a therapeutic response was manifest before the appearance of any toxic manifestations.

Ralph W. Danielson.

Zeppa, Rosario. **Changes in the curvature of the cornea after intervention for juvenile cataract.** Ann. di ottal. e clin. ocul. **75**:83-88, March, 1949.

In a series of 22 cases the ophthalmometer showed that after a discussion, if the needle was introduced at the limbus above, the curvature of the horizontal meridian was increased and that of the vertical meridian was usually decreased; whereas after aspiration, if the keratome section was made at the limbus temporally or nasally, the curvature of the vertical meridian was increased and that of the horizontal meridian was decreased. The decrease in curvature of the horizontal meridian after aspiration was proportional to the length of the section. In view of these predictable changes the operator has a means of limiting or reducing a pre-existing astigmatism by varying the point of entry and the length of the section. Harry K. Messenger.

6

OCULAR MOTILITY

Jaeger, Ernst. **Indications and contraindications for strabismus surgery.** Klin. Monatsbl. f. Augenh. **115**:43-46, 1949.

Diminished fusion faculty, abnormal innervation and abnormal position of rest are causes for strabismus. The choice of treatment depends on these causes. Indications for surgery are the possibility to restore binocular vision, psychic, social and occupational considerations and occasionally convergence in hyperopes who want to avoid glasses. Early age is no contraindication for surgery. The author's technique of guarded tenotomy and advancement is described.

Max Hirschfelder.

Lee, O. S., and O'Brien, C. S. **Surgical treatment of concomitant divergent strabismus.** Arch. Ophth. **42**:178-184, Aug., 1949.

Statistics were compiled from 49 consecutive operative cases of divergent strabismus in an effort to determine the amount of correction obtained by varying amounts of surgical alteration of the muscles. Results of operations in concomitant exotropia appear to be extremely variable, even with a standard technique. If the operation is confined to one eye it is difficult to over-correct the higher degrees of exotropia. Retinal correspondence appears to have no bearing on the surgical result. The exotropia of divergence excess and that of divergence excess plus convergence insufficiency apparently respond equally well to operation, and it is not necessary to differentiate the type of defect in order to decide on the operative procedure. In spite of the variable results, the following operations are advised. For exotropia of less than 10 degrees recession of the lateral rectus muscle in one eye from 4 to 7 mm. or approximately 1 degree of correction for each millimeter of recession, is indicated. For exotropia of 11 to 20 degrees one combines recession of the lateral rectus muscle (5 to 6 mm.) and resection of the medial rectus muscle (6 to 10 mm.) on one eye. One should expect approximately 1 degree of correction for each millimeter of change in the muscles. For exotropia over 20 degrees they suggest recession of the lateral rectus muscle (5 to 6 mm.) and resection (6 to 10 mm.) and advancement (2 to 3 mm.) of the medial rectus on one side. Approximately 1.5 degrees of correction may be expected from each millimeter of change in the muscles.

John C. Long.

Toselli, Carlo. **Isolated bilateral paralysis of the abducens.** Rasegna. ital. d'ottal. **18**:189-195, May-June, 1949.

Bilateral sixth nerve paralysis developed suddenly in a 25-year-old man following a severe headache which appeared at the end of an attack of influenza. The author considered the cause to be a toxic inflammation of the arachnoid sheaths of the abducens nerve in the space between the bulbopotine angle and the dura.

Eugene M. Blake.

7

CONJUNCTIVA, CORNEA, SCLERA

Allen, J. H., and Barrere, L. E. **Prophylaxis of gonorrheal ophthalmia of the newborn; comparison of effectiveness of penicillin and silver nitrate.** J.A.M.A. **141**:522-526, Oct. 22, 1949.

In this study, penicillin had no advantage over silver nitrate in the prophylaxis of gonorrheal conjunctivitis of the newborn. There is a diminishing incidence of Neisseria gonorrhea in cultures, from the antepartum cervix.

I. E. Gaynon.

Azzolini, U. **The pathogenesis of band-like keratitis.** Rassegna. ital. d'ottal. **18**: 171-181, May-June, 1949.

The various contributory factors which can be considered in the etiology and

pathology of bandlike keratitis are reviewed. Clinical and histologic studies do not warrant the division into primary and secondary types, dependent upon an antecedent uveal inflammation. The latter is to be considered a concommitant affection which may involve the uvea or the cornea, or both. Only very rarely are there familial or hereditary factors which justify considering the corneal disease as primary. The article presents an excellent statement of the changes in the epithelium, endothelium, aqueous, ocular tension, diffusion of fluids through the cornea and the biochemistry.

Eugene M. Blake.

Blumenthal, C. J. **Corneal graft in a European eye using a non-European transplant; report of a successful case.** South African M. J. **23**:840-841, Oct. 8, 1949.

A case of successful corneal transplantation is reported in which the donor cornea came from a 17-year-old African girl with absolute glaucoma and the recipient was a 19-year-old European girl with bilateral corneal scarring that in some respects suggested dystrophy.

I. E. Gaynon.

Carleton, A. **Vesicobullous diseases affecting the eye.** Brit. M. J. pp. 835-837, Oct. 15, 1949.

The similarity in the cellular reaction in vesicobullous diseases of the eye, regardless of cause, is brought to attention.

Donald T. Hughson.

Colditz, H. **Effect of oil of wintergreen on ocular pathogenic germs and on serpentic ulcer.** Klin. Monatsbl. f. Augenh. **115**: 57-63, 1949.

Oil of wintergreen, the methyl ester of salicylic acid, was effective in stopping advanced serpentic ulcer of the cornea. The drug was massaged into the cornea for three to five minutes with the aid of a spatula. The use of this drug is not suitable for small ulcers, but seems promising in serpentic ulcers with extensive damage to the corneal parenchyma. Bacteriologic experiments with the drug gave similar results as were obtained with optochin and proved to be bacteriocidal to pneumococci.

Max Hirschfelder.

Ferraris de Gaspare, P. F. **Experimental investigations of hydroquinone keratoconjunctivitis.** Boll. d'ocul. **28**:361-367, June, 1949.

Workers employed in hydroquinone manufacturing may develop keratitis and conjunctivitis. These lesions were studied in white and pigmented rabbits. After application of hydroquinone to the eye some were kept in the dark, others in average illumination, others exposed to sunlight, and some irradiated with ultra-violet light or exposed to sensitizing substances. The lesions observed in the conjunctivas and corneas of the rabbits were similar to those occurring in exposed workers. Illumination is an important factor in development of both experimental and industrial hydroquinone keratoconjunctivitis.

K. W. Ascher.

von Herrenschwand, F. **The treatment of tuberculous scleritis.** Ophthalmologica **118**:161-168, Sept., 1949.

The author recommends and gives detailed instructions for percutaneous tuberculin therapy by means of Ektebin ointment (E. Merck) which contains killed tubercle bacilli of human and bovine strains plus a tuberculin. Tuberculous scleritis is characterized by a torpid, almost painless course, circumscription and destructiveness of the lesion and the association with a chronic anterior uveitis. In the author's experience Ektebin had a reliable and almost electively good effect on the progress of the disease.

Peter C. Kronfeld.

Horowitz, S. **Psoriasis vulgaris: report on a case showing skin, joint and eye lesions (keratitis psoriastica).** Glasgow M. J. **30**:251-254, July, 1949.

The author reports a case of psoriasis vulgaris in a 63-year-old woman. In both eyes the nasal half of the corneae had a superficial vascularization beneath Bowman's membrane, a deep opacity at the center of the cornea and a corneal ulcer between the opacity and the vascularized corneal tissue. I. E. Gaynon.

Pavišić, Zvonimir. **A case of Salzmann's nodular dystrophy of the cornea.** Ophthalmologica **118**:169-172, Sept., 1949.

The author describes a typical case of this disease and discusses the differential diagnosis. Peter C. Kronfeld.

Pittar, C. A. **A preliminary note on a new method of fixing corneal grafts.** Brit. J. Ophth. **33**:567-573, Sept., 1949.

A splint was designed to seal the graft against leakage of aqueous and to prevent its tilting. A ring was made of thin sheet metal 1.5 mm. wide and of such a circumference as to overlap the trephine cut by 0.75 mm. on each side and with four arms 1.5 mm. wide which can be anchored by suture in the sclera or the cornea beyond the graft. It is made to conform to the corneal curvature. A second piece is made exactly as the first except that the aperture of the ring is made larger to conform to the size of the trephine blade; this is the trephine guide and is first sutured in place. It serves to place the graft exactly within the center of the splint and to place accurately the anchoring sutures for the arms of the splint. Morris Kaplan.

Thygeson, Phillips. **Acute trachoma.** Arch. Ophth. **42**:655-665, Nov., 1949.

Fourteen cases of trachoma with acute symptoms are reported and analyzed. In 5 of the 14 cases there was secondary bacterial infection which could have accounted for the acute symptoms, but in the remaining 9 the trachoma was uncomplicated. The large number of viral inclusions and the occurrence of free viral elementary bodies in the exudate suggest that the acute symptoms were due to the action of the trachoma virus itself. Trachoma, while ordinarily a chronic disease, sometimes has an acute phase. Pure acute trachoma in this series was characterized by extreme papillary hypertrophy of the conjunctiva, by a mucopurulent exudate in which polymorphonuclear leukocytes predominate, by an abundance of cytoplasmic inclusions in epithelial scrapings, and by a severe and extensive punctate epithelial keratitis. Ralph W. Danielson.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Vail, Derrick. **Subchoroidal expulsive hemorrhage occurring during thiopental sodium (sodium pentothal) anesthesia.** Arch. Ophth. **42**:562-566, Nov., 1949.

Vail reports the case of a 69 year old woman who had a retrobulbar hemorrhage after a retrobulbar injection for a cataract extraction. The operation was postponed for three days until there was no proptosis, increased intraocular tension, or limitation of movement of the eyeball. Because of the patient's nervousness and apprehension, it was decided to do the cataract extraction under sodium pentothal anesthesia. The blood pressure just before anesthesia was 160/80, it dropped to 130/80 at the beginning of the anesthesia and did not vary, even during the hemorrhage.

As soon as the incision with the Graefe knife was made, the wound gaped, and the lens, and then the vitreous, spontaneously began to extrude. On delivery of the lens the sutures were quickly tied. With

focal illumination a small, dark brown elevation, resembling a choroidal melanoma, could be seen. It increased rapidly in size. A posterior sclerotomy in the area of the choroidal elevation was quickly made and the knife blade twisted and held for three minutes. During this time a large amount of bright red arterial blood poured from the sclerotomy wound. A second sclerotomy was also done. During the event the patient showed no signs of surgical shock.

Two months later the corneal reflex was bright and no ocular congestion was present. The pupil was drawn up and there was a thick membrane in the pupillary space. The tension measured 14 mm. Hg (Schiøtz), and she had good light projection. Vail believes the hemorrhage came from the sclerotic posterior ciliary arteries. Ralph W. Danielson.

9

GLAUCOMA AND OCULAR TENSION

Duke-Elder, Stewart. **Fundamental concepts in glaucoma.** Arch. Ophth. **42**:538-545, Nov., 1949.

This article is too full to be properly abstracted. In part it is a plea to retain the conventional classification, namely, simple and congestive glaucoma. The author ably objects to the emphasis on the division of glaucoma into the narrow-angled and wide-angled types. The author would not decry the undoubted importance of the width of the angle in certain cases, but it is merely an anatomic peculiarity which sometimes influences the gravity of this complication. To make it the central pivot around which the subject of glaucoma hinges is a suggestion lacking in philosophy and full of practical pitfalls. Ralph W. Danielson.

Fanta, H. **Ocular hypotony due to vitreous in a cyclodialysis pocket.** Ophthalmologica **118**:205-207, Sept., 1949.

In the case reported a low-grade noncongestive glaucoma developed four years after an uncomplicated intracapsular cataract extraction. The position of the hyaloid membrane after the cataract operation had not been recorded. At the time of the discovery of the glaucoma the anterior chamber was found to be filled with vitreous. Since the glaucoma proved refractory to miotics, a cyclodialysis was performed through a trephine opening in the sclera (after von Sallmann). This operation was followed by lasting hypotony. Gonioscopic examination revealed a cyclodialysis pocket "kept open" by strands of shrunken vitreous which extended from the pocket through the anterior chamber into the center of the vitreous cavity. The case demonstrates the shrinkage that vitreous unprotected by the hyaloid membrane undergoes upon contact with the aqueous.
Peter C. Kronfeld.

Haik, G. M., Breffeilh, L. A., and Boggess, L. A. **Treatment of congenital glaucoma with beta radiation.** New Orleans M. and S. J. **102**:182-184, Oct., 1949.

An Iliff applicator containing 50 mg. of radium was applied over the ciliary body for a total dosage of 50 minutes at 9-o'clock and 30 minutes at 3-o'clock, in a case of hydrophthalmus. This brought the increased tension to normal after trephining had failed. I. E. Gaynon.

Di Luca, Giuseppe. **The cerebral circle in glaucomatous subjects.** Riv. oto-neuro-oftal. **24**:136-149, March-April, 1949.

In 40 patients with primary glaucoma, between 19 and 76 years of age, the behaviour of collateral compensation of the cerebral circulation was noted and controlled by means of manual compression of the common carotid artery against Chassignac's tubercle. All these patients showed a cerebral vasomotor lability and consequently greatly reduced power of

autoregulation of the cerebral circulation in comparison with normal subjects. These findings confirm the belief that glaucoma is a vascular disease involving not only the eye but all the cephalic segments of the circulatory system, with particular involvement of the carotid territory. This pathologic state of the ocular and cerebral circulation probably depends on neural, endocrine, vegetative, and endocranial disturbances, the latter in the thalamus, hypothalamus and hypophysis.

Melchiore Lombardo.

O'Brien, C. S., and Weih, J. **Cyclodialysis.** Arch. Ophth. **42**:606-619, Nov., 1949.

Cyclodialysis as an operation for the relief of increased intraocular pressure has gained in favor with the staff of the ophthalmologic clinic at the University of Iowa. Now it is the operation of choice for chronic noncongestive wide angle or narrow angle glaucoma, hydrophthalmus and certain types of secondary glaucoma, notably that after cataract extraction. The results, after at least one year of 100 consecutive operations on patients with chronic primary glaucoma, are reported.

As a rule, the superior temporal quadrant is chosen as the site of the operation. The conjunctival incision is approximately 8 mm. long, and parallel to the limbus and from 6 to 8 mm. from it. Before the incision is made, a scleral fixation suture of 0000 silk is placed just anterior to the area of intended incision. The area of incision is touched very lightly with a heated instrument to coagulate the vessels. The scleral incision is made approximately 4 mm. back of the limbus and is 3.5 to 4 mm. long. A special grooved spatula is used for the actual dialysis. As soon as the tip of the instrument is seen in the anterior chamber, the spatula is withdrawn slightly, and then, by repeated thrusts of the tip of the instrument through the region of the scleral spur, almost one-half the attachment of the ciliary body is torn loose. The sweeping motion as advocated by Heine, or that made in the opposite direction, as described by Blaskovics, is not used. The groove in the spatula is utilized to draw the blood from the area of operation during the few minutes in which bleeding usually occurs.

Immediately after operation 0.25-percent solution of physostigmine salicylate is instilled. Pilocarpine nitrate, 1-percent solution, is instilled twice a day. If undue redness develops or evidence of early iritis appears a 5-percent solution of cocaine hydrochloride and 1-percent epinephrine bitartrate jelly are instilled once a day. This medication dilates the pupil temporarily and prevents formation of synechias. Gentle massage, an important part of the postoperative treatment, is instituted on the day following operation and is continued twice daily for several weeks.

In 79 of the 100 cases the result was successful for at least one year. Only three cases of severe hemorrhage were encountered. There was some eventual diminution of visual acuity in 23 cases, usually as a result of cataract.

Ralph W. Danielson.

Phelps, G. D. **Incidence of glaucoma.** J. Iowa St. M. Soc. **39**:515-520, Nov., 1949.

Of 720 patients, all over the age of 45, 37 were found to have glaucoma, of which 18 patients had obvious glaucoma and 19 had hidden glaucoma. Routine tonometry of all patients over 45 years of age is advocated.

I. E. Gaynon.

10

CRYSTALLINE LENS

Barkan, Otto. **Operation for congenital cataract.** Arch. Ophth. **40**:680-684, Dec., 1948.

The traditional treatment of needling or discission of congenital cataract or

membrane is open to many serious objections. Removal of the cataract by a modified form of linear extraction is recommended. The technique is described in detail. Akinesia and extreme mydriasis are used. The keratome incision is a shelving one. The cataract or membrane is removed in one of a number of ways depending upon the type. After the operation the chamber is deepened by the injection of saline solution or air through a needle puncture made before the section. This technique makes it possible to carry out extraction in early infancy without undue hazards. (4 figures.)

John C. Long.

Hallermann, Wilhelm. **Unusual after-cataract present in both eyes.** Klin. Monatsbl. f. Augenh. **115**:51-53, 1949.

Calcified embryonal suture lines with several layers of lenticular lens remnants were found in front of the iris in both eyes of a child who had been operated on several years before for congenital cataract. (2 figures.)

Max Hirschfelder.

Kirby, D. B. **Preparation of the whole patient for cataract surgery.** Irish J. M. Sc. pp. 707-714, Sept., 1949.

The importance of considering the various aspects of the prospective surgical patient's health is stressed by the author. The general and local complications that commonly arise both immediately and postoperatively are enumerated, and the writer's methods of avoiding these hazards are discussed in detail.

Donald T. Hughson.

Laval, Joseph. **A simple and efficient cataract suture.** Arch. Ophth. **42**:189-191, Aug., 1949.

The technique of the cataract suture is as follows: A conjunctival incision is made 5 mm. from the limbus for one-half the circumference of the cornea, and the corneoscleral junction is exposed in the region of 12 o'clock. A keratome incision about 5 mm. long is made at this point. One needle of a double-armed suture is passed through the outer layers of the scleral lip of the keratome wound, the point toward the surgeon. The other needle is passed through the corneal lip of the keratome wound, the point away from the surgeon. The first needle is then brought through the conjunctiva. The section is enlarged with scissors. The conjunctiva is closed with a running silk suture. This technique has the advantage that the corneoscleral suture is inserted when the chamber is opened by only the relatively short keratome incision.

John C. Long.

Pau, Hans. **Decrease of cataract morbidity in old people.** Klin. Monatsbl. f. Augenh. **115**:53-55, 1949.

Comparing the type of cataract operated on at the Düsseldorf Eye Hospital with the number of people in various age groups of the city's population the author found that cortical cataracts increase in age groups from 40 to 80 years of age. After that age the incidence of cortical cataract declines and the number of nuclear and sclerosed cataracts increases. He points out that progressive sclerosis of the lens nucleus bars opacification of the lens cortex. (1 curve, references.)

Max Hirschfelder.

Pillat, A. **Intracapsular extraction of cataracta complicata accreta after iridocyclitis and glaucoma.** Arch. Ophth. **42**:567-582, Nov., 1949.

The operation for cataracta accreta following iridocyclitis was a source of anxiety to the surgeon and of danger to the patient's eye before the introduction of the intracapsular method by Arnold Knapp. The author reports on an unse-

lected series of 105 intracapsular extractions for cataracta complicata accreta after iridocyclitis which were performed in his clinic from 1945 to 1949. In 63 patients the cataract came after iridocyclitis, in 30 after operation for glaucoma with posterior synechias, in 5 after iridocyclitis traumatica, in 5 with Fuchs's heterochromia, and in 2, with aplasia of the iris. Of the 98 eyes with cataracta complicata in the first three groups, 86, or 87.7 percent, could be operated on intracapsularly. Useful vision was obtained in a high percent. The present series of nearly 100 intracapsular cataract operations for cataracta accreta demonstrates that eyes with such severe damage tolerate the intracapsular extraction exceedingly well, that the healing of the wound proceeds smoothly, that the number of complications is not greater than in operations for senile cataract and that in this series of 105 operations an eye was destroyed by an infection only once. The author's technique is described. Loss of vitreous must always be expected in eyes with uveal disease.

Ralph W. Danielson.

Winkler, Gerhard. **Is there a spindle-shaped cataract? (Cataracta fusiformis)** Klin. Monatsbl. f. Augenh. **115**:46-51, 1949.

In the older literature spindle-shaped cataract is described as a form of congenital opacity which penetrates the lens from the anterior to the posterior pole axially. Since the advent of the slitlamp it has become evident that no true fusiform cataract exists and that one can find a clear central part within the lens nucleus in all cases formerly described as spindle-shaped cataract. The embryonal development of the lens makes the formation of an axial cataract impossible.

Max Hirschfelder.

11

RETINA AND VITREOUS

Benedict, W. L. **The clinical significance of closure of the retinal vessels.** J.M.A. Georgia **38**:423-433. Oct., 1949.

Unilateral thrombosis of the central retinal vein occurs in individuals beyond the age of 50 who suffer from sclerosis of the peripheral arteries, mild hypertrophy of the left ventricle, and probably pulmonary emphysema. Closure of the central retinal artery may be due to spasm, organic thickening of the wall or to generalized narrowing of the arterioles. Occlusion without hypertensive findings may be assumed to be due to an embolus. Retinal arteriosclerosis is a part of hypertensive disease and diffuse arteriosclerosis. I. E. Gaynon.

Caccamise, W. C. **Congenital nonprogressive night blindness.** U. S. Army Med. Dept. Bull. **9**:920-928, Nov., 1949.

Oguchi's disease is a congenital abnormality which is manifest as a nonprogressive night blindness with characteristic eyeground findings. The discs are normal but seem dark in contrast to the surrounding pale retina. The fundus has pale gray areas that are sometimes mixed with yellow. The vessels appear dark in the pale areas and in such areas the difference between arteries and veins is not distinct. On one side of the vessels a dark shadow appears and on the other a marked white reflex. The choroidal vessels are not visible. After the eye has been covered, the fundus takes on a normal appearance and after exposure to light the original appearance returns. This is the first extensive review in English.

I. E. Gaynon.

Graveson, G. S. **Retinal arterial occlusion in migraine.** Brit. M. J. pp. 838-840, Oct. 15, 1949.

Three cases of occlusion of a branch artery and one with central retinal arterial occlusion as a concurrence of migraine are reported, and the mechanism of migraine discussed.

Donald T. Hughson.

Landau, J., Bromberg, Y. M., Birnbaum, D., and Feigenbaum, A. **Manifestations of shock in the fundus of the eye.** Acta Med. Orientalia **8**:1-12, Jan.-Feb., 1949.

In 18 of 20 patients in shock after war injury, a characteristic fundus picture was observed. The most frequent manifestation and the one that disappears last in recovery is an arteriolar constriction which is followed by venous hyperemia. In mild cases slight turbidity of the retina is seen in the periphery and macula. In severe shock, there is a loss of transparency of the entire fundus which varies from barely perceptible turbidity to frank edema.

F. H. Haessler.

Leatham, Aubrey. **The retinal vessels in hypertension.** Quart. J. Med. **18**:203-216, July, 1949.

Examination of the retinal vessels will be of distinct aid in the diagnosis of hypertension when only one clinical examination is possible, because the state of the retinal arterioles is a more stable indication of the blood pressure than the blood pressure reading, when the blood pressure has fallen from a high level, often after cardiac infarction, and in the investigation of obscure cardiac enlargement with normal blood pressure at the time of observation. The retinal arterioles of 214 patients have been examined. One-hundred-eleven of them had hypertension of varying degree and 103 were normal controls. Among the controls 14 persons were over 65 years of age. Irregularity of the lumen and generalized narrowing of the retinal arterioles are the most characteristic signs of hypertension. Pallor of the arteriolar blood column, arteriovenous crossing, broadened or exaggerated light reflex, although seen in hypertension, are found in healthy persons too. High diastolic pressure was found to cause changes in the retinal arterioles more often than high systolic pressure with normal diastolic. Nevertheless, in about 10 percent of patients with a diastolic pressure of 110 mgm. or over, the retinal vessels were within normal limits. Changes in the retinal arterioles were found more often in hypertensive patients with radiologic evidence of enlargement of the left ventricle and left ventricular preponderance in the electrocardiogram than in patients without these signs of cardiovascular hypertrophy.

R. Grunfeld.

Lindner, K. **Shortening of the eyeball for detached retina.** Arch. Ophth. **42**:634-645, Nov., 1949.

Lindner outlines the difficulties and techniques of this operation. During the years 1944 and 1945 the shortening operation was performed on 36 eyes at his clinic. At the time of the patient's discharge from the hospital 6 eyes were cured, 10 were improved, the condition of 9 was unchanged, and that of 11 was worse. Twenty eyes were shortened once, 12, twice, and 4, three times. Only some of the patients could be reëxamined two or three years later. In several of the eyes which were cured the improvement of function was slight. As a rule, when the retina has been detached for a long time, one year is required for the attainment of the final functional result.

Ralph W. Danielson.

Pines, N. **The artificially produced retinal pulse.** Brit. J. Ophth. **33**:579-583, Sept., 1949.

External pressure on the eyeball frequently causes a pulsation of the arteries of the disc. They empty in diastole and fill in systole. If the pressure on the eye

is increased greatly, it is possible to cause a collapse of the disc arteries which is followed shortly by a narrowing or collapse of the veins. This increased pressure which is very painful collapses the arteries in the disc and a disc diameter beyond, but the retinal vessels do not collapse no matter how much pressure is applied. This is explained by the fact that the column of blood is forced out of the large disc arteries and into the retinal arteries but cannot be forced out of the latter smaller vessels because the capillary bed acts as a buffer which impedes the movement of the blood column.

Morris Kaplan.

Vail, Derrick. **Treatment of angiomatosis of the retina (Von Hippel's disease).** Quart. Bull. Northwestern Univ. Med. Sch. **23**:397-400, 1949.

Angiomatosis retina is amenable to treatment before the secondary stages set in. The most efficient therapy is that of surface diathermy or ignipuncture of the lesion itself. The author used a 1.5 mm. needle for ignipuncture at 40 milliamperes for four seconds. After the lesion has been destroyed, it takes at least a year for the secondary lipoid changes to disappear. I. E. Gaynon.

Velhagen, K., Jr. **The clinical significance of vitreous prolapse into the anterior chamber.** Ophthalmologica **118**: 173-181, Sept., 1949.

In a lucid and concise manner Velhagen reviews the well known clinical implications and complications of prolapse of vitreous into the anterior chamber. The main dangers are ocular hypertension and clouding of the cornea. For the latter Velhagen recommends paracentesis and air injection into the anterior chamber. The recent papers by P. Chandler and A. D. Reese seem to have escaped the essayist's attention.

Peter C. Kronfeld.

12

OPTIC NERVE AND CHIASM

Allen, T. D., and Seidelmann, O. F. **Allergic retrobulbar neuritis.** Illinois M. J. **96**:106-109, Aug., 1949.

Retrobulbar neuritis with relative and absolute paracentral scotomas occurred in a patient who was sensitive to tomatoes, strawberries, bananas, camel's hair, cat's hair and staphylococcus. Marked improvement followed the avoidance of the allergens and pyrobenzamine therapy.

I. E. Gaynon.

Bray, E. R. **Tumors of the optic disc.** Minnesota Med. **32**:809-810, Aug., 1949.

A case of drusen of the optic nerve associated with adenoma sebaceum in a mentally normal 12-year-old boy is reported. I. E. Gaynon.

Gát, L., and Mándi, L. **Ophthalmoscopic findings with BCG-vaccination.** Szemészet **3**:165-170, 1949.

The authors found a tuberculo-allergic papilloretinitis in 12.7 percent of 110 persons free of complaints and active pulmonary changes. Five of the patients reacted to tuberculin whereas the tuberculin test was negative in one and doubtful in one. In 53 patients with negative fundus findings the number of tuberculin positive and tuberculin negative individuals was nearly equal.

Twenty-five persons who had not reacted to tuberculin were inoculated with BCG vaccine. In 15 of them papilloretinitis, developed after 8 to 12 weeks. In 12 of the latter group the tuberculin test was repeated 8 to 12 weeks later with positive results. On the basis of these data there is an indisputable correlation between the occurrence of tuberculous allergy and the papilloretinitis reported. Tuberculo-allergic papilloretinitis can be similarly observed with miliary tuberculosis, tuberculous meningitis, extensive cavernous phthisis, benign primary infections, oc-

cult tuberculosis, and in those persons who had been inoculated with BCG two to three months previously. This pattern is a transient sequel of tuberculous oversensitivity rather than a symptom of tuberculous meningitis or any specific toxicosis. Gyula Lugossy.

Igersheimer, Joseph. **Atrophy of the optic nerve in tabes and dementia paralytica.** Arch. Ophth. **42**:170-177, Aug., 1949.

The author, with wide experience in examining anatomical material, states that in attempting to explain the pathogenesis of atrophy of the optic nerve in tabes and in dementia paralytica, the following points should be borne in mind. 1. The atrophy always starts in the marginal zone, near the pial sheath, and therefore the causative agent enters from the meninges. 2. Degeneration has been seen in the earliest stages, without any sign of exudation; on the other hand, degenerative and infiltrative processes exist together, and inflammatory signs in the intracranial portion of the nerve are frequently present without any atrophy. 3. Treponemes are located in the arachnoid and pia of the optic nerve and never in the neural parenchyma. 4. Antisyphilitic drugs generally have no healing or arresting effect on the optic nerve atrophy in tabes and dementia paralytica, whereas they may influence decending optic nerve atrophy in basilar syphilitic meningitis. Behr's hypothesis considers that basilar syphilis is a disease of the mesodermal tissue, and the optic nerve atrophy is due to a syphilitic optic neuritis involving the intracranial portion of the nerve. (6 figures.) John C. Long.

Oxilia, E. **Congenital anomalies of the fundus oculi: marginal veins of the optic nerve and hyaloid rests.** Ann. di ottal. e clin. ocul. **75**:20-29, Jan., 1949.

From his study of an eye with hyaloid rests and a marginal vein of the optic nerve, Oxilia concludes that the incomplete absorption of the neurogliar sheath of the hyaloid artery and the consequent presence of fibrous tissue on the nerve head may account for the anomalous papillogenesis, as the vein is prevented by the fibrous tissue from attaining its normal axial position on the papilla. (2 figures.) Harry K. Messenger.

Scuderi, G. **Melanoblastoma of the papilla.** Boll. d'ocul. **28**:321-338, June, 1949.

Melanoblastomas of the optic nerve head are rare; one case in a 51-year-old woman is described. The tumor was unilateral, almost round, 1½ times as wide as the disc, and blackish-gray with lighter spots. The highest elevation was about three diopters. Intraocular pressure was normal. Visual acuity was 1/60, and there was a gun barrel field. After enucleation, the histologic examination revealed an intensively pigmented melanoblastoma of the disc, perforation of the lamina cribrosa and invasion of the distal part of the optic nerve. The origin of the tumor was assumed to be neuro-ectodermal. (10 figures, 35 references.) K. W. Ascher.

13

NEURO-OPHTHALMOLOGY

Cardello, Giovanni. **Ocular symptoms in subarachnoid hemorrhage.** Rassegna ital. d'ottal. **18**:182-188, May-June, 1949.

Two forms of subarachnoid hemorrhage are recognized, one appears suddenly in an apparently healthy person, like an apoplexy, and in the other there is a prodromal period of ill health, especially head pain. The former is usually fatal and due to rupture of an aneurysm; patients with the latter generally recover. When there are no localizing symptoms the extraocular motor nerves are almost always involved. Fundus changes occur

frequently. Two cases are reported in the first of which the picture was that of a serous meningitis with edema of the optic disc and retinal hemorrhages. The second patient rapidly developed an extreme edema of the orbit, so that the eyes were fixed, and a retinal hemorrhage with intense edema resembling a detachment. Death occurred promptly.

Eugene M. Blake.

Venco, L., and Morone, G. **The syndrome of Adie.** Rassegna ital. d'ottal. **18**: 137-162, May-June, 1949.

Attention is called to the fact that the syndrome bearing Adie's name has been previously described by many others and that several atypical forms are known. Four cases are described which were studied clinically and pupillographically, two of which were typical and complete, one atypical and one incomplete form of pseudotabetic pupillotonia. In the first two instances there was absence of knee and Achilles reflexes, in the third the absence of such reflexes was accompanied by pupillary reaction to normal luminous stimuli. The fourth cases presented the typical tonic pupils but overaction of the leg reflexes. None of the patients was syphilitic.

Pupillographic studies are reported which confirm the findings and demonstrate the behavior of the pupils to miotics and mydriatics. The authors suggest that the pupillary changes result from the interference of the intercalary structure in the region of the third nerve nucleus, and that the tendon reflex behavior depends upon changes in the spinal cord.

Eugene M. Blake.

Walsh, F. B. **Bilateral total ophthalmoplegia with adenoma of the pituitary gland.** Arch. Ophth. **42**:646-654, Nov., 1949.

This paper contains the findings in summary form in 50 consecutive cases of verified pituitary tumor seen in the Johns Hopkins Hospital, a brief report of two cases of bilateral ophthalmoplegia, a diagram which illustrates the possible routes of spread of adenoma of the pituitary gland, and comments on involvement of the fifth nerve as part of the syndrome of the cavernous sinus.

Particular mention is made of the absence of demonstrable involvement of the fifth nerve in the two cases of ophthalmoplegia associated with pituitary tumor. If pressure on the cavernous sinuses is the proper explanation of ophthalmoplegia in these cases, it is difficult to understand why the first and second division of the fifth nerve were not affected. Certainly, these sensory branches of the fifth nerve are as available for pressure as are the other (motor) nerves. Experimental work by Denny-Brown seems to establish a factual explanation. He found that with carefully controlled cuff pressure he could abolish the function of motor nerves before that of sensory nerves. The sequence of events from pressure is probably paresthesias, motor loss and sensory loss.

Ralph W. Danielson.

14

EYEBALL, ORBIT, SINUSES

Benedict, W. L. **Sarcoidosis involving the orbit.** Arch. Ophth. **42**:546-550, Nov., 1949.

This report is based on two cases of sarcoidosis of the orbit which were observed at the Mayo Clinic in 23 years. They are the only instances of sarcoidosis encountered in more than 1,000 cases of tumor of the orbit. Orbital complications have not occurred in any of the other cases of sarcoidosis at the clinic, but intraocular manifestations, such as iritis, chorioretinitis and uveitis, have frequently been present. Sarcoidosis is characterized histologically by a granulomatous, tuberculosis-like lesion which

contains epithelioid and multinucleated giant cells but is not associated with caseation necrosis. Some investigators believe that sarcoidosis is a separte disease entity of unknown origin, while others believe that it is a form of non-caseating tuberculosis. A diagnosis of sarcoidosis is made when animal inoculation, bacterial culture and other tests fail to disclose any etiologic agent.

Ralph W. Danielson.

Benedict, W. L. **Diseases of the orbit.** Tr. Am. Acad. Ophth. pp. 26-36, Sept.-Oct., 1949.

The clinical evidences, pathologic changes and causation of many orbital abnormalities are coördinated. Etiologies are classified as: congenital, vascular, neoplastic, inflammatory and endocrine. To facilitate diagnostic accurancy the orbit is divided into three surgical zones and three anatomic divisions. The first zone extends posteriorly to the equator of the globe; the second to 10 mm. behind the globe where the retinal vessels enter it; the third posteriorly to the orbital apex. The first anatomic division includes the tissues peripheral to the subperiosteum; the second the tissues between the periosteum and the muscle cone; the third the contents of the muscle cone. In the first division cranial meningiomas are the most frequent neoplasm; roentgenographic findings of hyperostosis suggest a vascular or neoplastic lesion in this zone. In the second division numerous space-taking lesions of vascular and neoplastic origin may occur. Space-taking lesions within the orbital cone are characterized by proptosis directly forward with possible visual involvement from optic nerve pressure. Here endotheliomas are most frequent and neoplasms are mostly primary. Space-taking lesions may become as large as the globe itself before producing appreciable proptosis. Hemangioma is a relatively frequent lesion and recurrence of the proptosis suggests a thrombosed aneurism. The injection of radiopaque substances should be used only by those who are thoroughly familiar with the technique and risks. Space taking lesions within the muscle cone are frequently associated with retinal wrinkling from pressure, choked disc, and visual loss. The most favorable surgical approach to lesions in the posterior zone is transcranial. The advisability of X-ray therapy in vascular orbital tumors is questionable except when surgical treatment is contraindicated. The Birch-Hirschfeld classification of orbital pseudotumors is explained and illustrated. Surgical intervention is seldom necessary in acute orbital cellulitis in small infants. Orbital abscesses are preferably drained by an incision through the upper lid at the middle of the upper orbital rim which is extended backward along the roof of the orbit into the middle zone. Among the less frequent causes of orbital inflammations are typhoid, coccidiosis, tick fever, some rickettsias and virus diseases, tularemia and sarcoid. Cases with apparent allergic reactions in the orbit have been reported. Watchful waiting and careful study is advised in doubtful diagnoses. Seldom does an orbital disease require emergency treatment. The use of X ray as a diagnostic and therapeutic measure in conditions of doubtful diagnosis is advised. The routine removal of orbital tissue for biopsy as a diagnostic procedure alone is deprecated.

Chas. A. Bahn.

Cogan, D. G. **Endogenous intraocular fungous infection.** Arch. Ophth. **42**:666-682, Nov., 1949.

Eleven cases of endogenous intraocular fungous infection have previously been reported. Of these, the causative organism was a blastomycete in three cases, an actinomycete-like organism in three and a cylindric branching fungus thought to

be A. fumigatus in five. An additional case, apparently in the aspergillus group, is described. The onset was characterized by loss of vision, redness, chemosis and proptosis without any evidence of systemic disease. The tension, which was low at first, became elevated, and the eye was removed because of pain. Histologically abscesses, with many giant cells, were found in the vitreous and in the inner portion of the retina. Near the abscesses, and often within their centers, were the fungus particles, consisting of dichotomously branched cylindric bodies which rarely had septums. Excrescences on the walls of these hyphae were interpreted as manifestations of disintegration. Ralph W. Danielson.

Pessagno, A. **Axial stratigraphic study of the normal orbit.** Ann. di ottal. e clin. ocul. **75**:210-215, June, 1949.

Roentgen-ray studies are presented of the normal orbit photographed according to Vallebona's axial stratigraphic method (transverse pluridirectional stratigraphy), whereby any desired layer or section of the orbit is visualized and photographed to the exclusion of other layers. Five stratigrams are shown. Pessagno proposes to apply the results of his studies to the field of orbital pathology, with particular reference to the differential diagnosis of tumors, in which stratigraphy promises to be of great value. Harry K. Messenger.

Petit-Dutailis, D., Feld, M., and Taptas, J. **Unilateral exophthalmos caused by orbital malformation in Recklinghausen's disease.** Rev. Neurol. **81**:203-211, March, 1949.

Two cases of unilateral exophthalmos are described, caused by malformation of the orbit as part of the associated Recklinghausen's disease. One was associated with pulsation and bruit but an arteriogram eliminated retroörbital tumor or aneurysm of the carotid artery. In the other, an enlarged orbit was associated with widened sphenoid fissure and enlarged optic canal and the sella turcica was sagittally enlarged. These findings led to the erroneous assumption of a retroörbital tumor. Exploratory operation did not reveal any tumor in the pituitary region but a right parietal meningioma.
R. Grunfeld.

Redslob, E. **The danger of incorrect evisceration and enucleation.** Ann. d'ocul. **182**:768-773, Oct., 1949.

After a brief discussion of the esthetic factor in correctly and incorrectly performed eviscerations and enucleations, the indications are presented. Some of the indications for enucleation are potential sympathetic ophthalmia, intraocular tumors, some hemorrhagic diseases, and deformities of the globe. It is important to avoid undue trauma of the orbit. Sympathetic ophthalmia and tumors as a result of incomplete removal of sclera and choroid have been observed. In panophthalmitis, evisceration, which is essentially an emergency operation, is indicated and all uveal pigment should be removed from the scleral shell. Chas. A. Bahn.

Robertson, E. G. **Pulsating exophthalmos due to defective development of the sphenoid bone.** Am. J. Roent. and Radium Therapy **62**:44-51, July, 1949.

A case of unilateral, pulsating exophthalmos due to defective development of the bony wall of the orbit is reported.
Donald T. Hughson.

15

EYELIDS, LACRIMAL APPARATUS

Butler, J. B. V. **A simple operation for entropion.** Arch. Ophth. **40**:665-667, Dec., 1948.

The mechanism of the development of spastic entropion is discussed. A new

operative procedure for the correction of this condition is described. The inferior edge of the tarsus is shortened by the removal of a triangular wedge. This causes the inferior portion of the tarsus to hug the globe and thus prevents entropion. The surgery is done under local anesthesia. An incision is made from the conjunctival surface at the lower border of the tarsus and the orbicularis freed from the tarsus. A wedge-shaped piece of tarsus is then excised. The base of the wedge is the inferior tarsal margin. The tarsal defect is then closed with two sutures. (1 figure.) John C. Long.

Couzi, Jacques. **Meibomian conjunctivitis, blepharoconjunctivitis and blepharitis.** Ann. d'ocul. **182**:761-767, Oct., 1949.

95 percent of chronic resistant conjunctivitis is primarily seborrheic. The oily meibomian secretion together with the alkaline tears may form a soap-like substance which is irritating to the eye. The glands of the outer third of the lower lid are most frequently involved. Secondary infection, especially with staphylococci, and an allergic neurovascular aggravation are frequent. In the noninfected type, expression of the meibomian secretion and instillation of a collyrium containing sodium borate and vasoconstrictors are advised. In severe cases diathermic coagulation of the worst affected meibomian glands is suggested. The procedure is similar to that for the removal of lashes. An ointment containing penicillin is used in the treatment of the infected form until the infection subsides.

Chas. A. Bahn.

Friede, R. **Clinical appearance and etiology of epicanthus.** Klin. Monatsbl. f. Augenh. **115**:12-27, 1949.

The formation of epicanthus can only be satisfactorily explained on the basis of phylogenetic development which repeats itself during the development of the human embryo. In this article the phylogenetic development of the lids is followed from the thickened ring of the fishes through the mammals to man, and the differences in various human races are pointed out. Medial epicanthus is found only in man. It is caused by a hypoplasia of the nose, a flattened nasal root and by pathologic variations of the intraorbital septum. Presence of abundant subcutis with loose periostial attachment and a preponderance of horizontal tissue tension in the palpebral diaphragm before puberty are a further necessity for its formation. The author distinguishes between pathologic and physiologic epicanthus. In both one finds a stopping or slowing down of the early development of the lids which remain in an early embryonic form and change only in size, but not in shape, during later stages of development. Pathologic epicanthus can be an isolated finding or may be accompanied by ptosis and signs of generalized dysplasia. Clinical instances are shown in the article. Physiologic epicanthus is temporarily manifest in a certain percentage of infants and in certain human races. A latent form becomes evident if the skin between brow and cheek is put under tension. (20 figures.)

Max Hirschfelder.

Heinsius, E. **Experiences with lid plastics.** Klin. Monatsbl. f. Augenh. **115**:35-40, 1949.

Cicatricial ectropium and entropium are best repaired by a free Thiersch transplant of epithelium. The Kreibig skinflap from the forehead is recommended for total substitution of lids. Cicatricial coloboma of the lids requires a careful preparation of the several layers in the lids and separate suturing of each layer. (12 figures, references.)

Max Hirschfelder.

Loehr, K. **A case of blepharochalasis in childhood.** Klin. Monatsbl. f. Augenh. 115:28-31, 1949.

A seven-year-old boy had recurrent lid edema and conjunctival and subcutaneous hemorrhages since the age of four. He developed a very atrophic skin in the lids with shrinkage of the subcutaneous fat. Vasolability and, possibly, endogenous allergy, are possible causes for this early case of blepharochalasis. (1 figure, references.) Max Hirschfelder.

Nichelatti, Paolo. **Sarcoma of the lacrimal sac. Roentgenotherapy. Three-year cure.** Ann. di ottal. e clin. ocul. 75:3-9, Jan., 1949.

Nichelatti presents a case, the fifteenth known, of primary sarcoma of the lacrimal sac. This small round-cell sarcoma, growing in an 18-year-old man, was the size of a small walnut and had already invaded extensively the surrounding tissue when it was treated with a total of 3150r in 21 sessions. After three years the region of the sac appeared quite normal except for the small biopsy scar. The differential diagnosis of sarcoma of the sac is clinically difficult, and only the absence of pain served to distinguish it from an early acute dacryocystitis.

Harry K. Messenger.

Schoepfer, Otto. **A simple procedure for cure of spastic entropium.** Klin. Monatsbl. f. Augenh. 115:40-42, 1949.

Three double armed sutures are introduced into the lower conjunctival fornix and brought out through the lid margin in line with the eye lashes. After having been tied tightly over a piece of gauze the sutures correct the spastic entropium. Scar tissue formation keeps the correction a permanent one, after the sutures are removed on the tenth day. (5 figures, references.) Max Hirschfelder.

Sidi, E., and Dobkevitch, S. **Dermatitis of the lids due to drugs.** Arch. d'opht. 9:311-320, 1949.

The authors call attention to the frequency of medication eczemas of the eyelids and note that these inflammations often continue weeks or months without the patient's recognizing the causal role of the collyrium or ointment. They describe the dermatitis and note that pruritis is the outstanding symptom. The importance of patch tests in the recognition of the offending drug is stressed but with a recommendation for caution in using them because of the possibility of a flare-up of the primary dermatitis. In view of this danger the tests should not be made while the dermatitis is active.

The authors noted the frequency of sensitization to the synthetic anesthetics and the infrequency of sensitization to cocaine. They made the observation that a patient sensitive to one of the sulfonamides or to paraphenylenediamine was very likely to be sensitive to one or more of the anesthetics also. The treatment of eczemas of the lids consists primarily in suppression of the offending medication, but daily applications of 1.5-percent silver nitrate solution and finally ichthyol ointment are of supplementary value. In case of severe secondary infection, antibiotic therapy may be necessary.

Phillips Thygeson.

16

TUMORS

Bors, M., and Nagy, I. **Cancer in the eye and its protecting organs.** Szemészet 3:170-175, 1949.

This is a summarising report based on the material of 28 years in the Ophthalmologic Department of Szeged University. Further, the case of a man aged 53 years is reported in whom choroid metastases of the cancer of a bronchus occurred. On necropsy, a primary cancer of

a left bronchus and generalised carcinomatosis was found. The metastasis in the right choroid was 14 mm. wide and 8 mm. thick, seated at the posterior pole. In the left eye, there was a circular infiltration of the choroid 12 mm. in length and 7 mm. in its greatest width.

Gyula Lugossy.

Brognoli, C. **The endotheliomas of the conjunctiva.** Boll. d'ocul. **28**:349-360, June, 1949.

A 4-year-old child had a sharply outlined, soft, movable, yellowish pink tumor, 3 by 2 mm., at the 3-o'clock position of his left corneal limbus. Histologic examination revealed an endothelioma consisting of parallel cell ribbons. The cells were fusiform and closely crowded; no proliferative signs were noticed. (2 figures, 31 references.) K. W. Ascher.

François, J., Kluyskens, J., and Rabaey, M. **Plasmocytoma of the orbit.** Ann. d'ocul. **182**:729-739, Oct., 1949.

Only three cases of this rare orbital neoplasm have been reported. The patient, a 77-year-old man, noted a slowly progressive exophthalmus of the left eye during one year. One year before he had been struck over the left orbit with a hammer. Vision was reduced to light perception. With X-ray therapy the growth markedly diminished. Microscopically the tumor was circumscribed and consisted almost entirely of plasmocytes. These had a diameter of 8 to 15 μ, were round or oval and had eccentric nuclei. In the conjunctiva plasmocytoma usually is secondary to chronic inflammations, especially trachoma. In the orbit, however, it is a primary tumor and rarely malignant. Chas. A. Bahn.

Loewenstein, Arnold. **Some aspects of ocular melanotic growth.** Brit. J. Ophth. **33**:525-543, Sept., 1949.

There is much controversy over the exact origin of melanotic growths of the eye. For many years it was generally accepted that they all arose from the mesoderm and in 1925 Dawson attempted to prove that they originated in the hexagonal layer of the ectoderm. Masson's work showed that these tumors arise from Schwann's sheath of the nerve fibers and Theobald, in 1937, proved that in five cases of malignant choroidal melanoma the tumor arose from the long posterior ciliary nerves. Now Loewenstein describes his histologic study of various pigmented tumors and the results generally bear out the belief that many arise from nerve sheaths but leaves in much doubt the origin of many more. Choroidal naevi are certainly more frequent than is assumed or than the scanty literature suggests. There is practically no possibility of a differential diagnosis between a beginning malignant melanoma and an innocent nevus clinically and such a diagnosis is frequently not even anatomically easy. Ophthalmoscopic control with repeated fundus photography seems to be the most sure way to discover the first sign of growth. Retinal degeneration directly over the choroidal tumor is frequently seen and may be used as a diagnostic criterion since it is not present over the subretinal fluid found adjacent to the tumor. (11 figures.)

Morris Kaplan.

Miles, P. W., and Dixon, J. M. **Tuberous sclerosis in three siblings.** Arch. Ophth. **41**:473-480, April, 1949.

Tuberous sclerosis is a familial heredodegenerative disease characterized by tumors in the brain, retina and skin, and sometimes other organs. The authors describe tuberous sclerosis in three siblings, all of whom had retinal lesions, radiopaque lesions of the brain, abnormal electroencephalograms and epileptiform seizures. The children were aged 10 years, 8 years, and 22 months. The two older

children had adenoma sebaceum and other abnormalities of the skin. The 10-year-old girl had normal mentality, but the 8-year-old boy's mental development was retarded two or three years. There is no family history of the disease, but the father had an anomaly of the retinas. The small retinal tumors observed in these three eyes could easily have been overlooked. John C. Long.

Pfeiffer, R. L., and Nicholl, R. J. **Dermoid and epidermoid tumors of the orbit.** Arch. Ophth. **40**:639-664, Dec., 1948.

Because there is little embryologic and histologic distinction between dermoid and epidermoid growths, the term "dermoid" is suitable for both. Intermediate or transitional types are common. The authors report in detail nine cases of dermoid which involved the orbit and caused exophthalmos. All were cystic, the epithelial linings varied greatly in number of layers and appearance of cells and the cavities contained fluid and semisolid matter. Hair was found in only one. This series is presented to call attention to defects produced in the bone which may be well studied by roentgenography, and which serve to distinguish these tumors from other causes of proptosis. The roentgenographic characteristic is an area of diminished density with smooth, regular margins of increased density.
John C. Long.

Samuels, Bernard. **Detachment of the retina in early sarcoma of the choroid.** Arch. Ophth. **42**:620-627, Nov., 1949.

Detachments of the retina associated with early malignant melanoma of the choroid have been divided by A. Fuchs into types, the minimal and the oral. The former is present on the opposite side of the eye and the oral occurs at the ora serrata. To the reported 11 cases the author adds 19 which were selected from the collection of sarcomatous globes in the museum of the Eno Laboratory at the New York Eye and Ear Infirmary.

The clinical recognition of minimal retinal detachment is difficult, particularly since there are no folds in the retina because the underlying fluid is too shallow to permit them to form. However, the transparency of the retina may be so impaired as to cause the markings of the choroid to be indistinct. A reduction in the field for blue corresponding to an area distant from the tumor should arouse suspicion of a minimal detachment. With careful search one may discover an oral detachment, using indirect ophthalmoscopy. Minimal detachments of the retina and those at the ora serrata are so characteristic of early sarcoma of the choroid as to be of pathognomonic importance. Ralph W. Danielson.

Simonelli, Mario. **Malignant melanoma of the iris.** Giorn. ital. oftal. **1**:481-497, Nov.-Dec., 1948.

The author describes a malignant melanoma of the iris in a man, 35 years of age, caused by a neoplastic transformation of a benign pigmented nevus. The first symptom was a spontaneous hemorrhage in the anterior chamber. Enucleation of the bulb was performed before infiltration of the tumor into the ciliary body. Histologic examination revealed malignant melanoma and spindle cells originating from the stroma of the iris.

The author summarizes the most recent findings on the histogenesis of melanotic tumors and points out that Masson has evidence which suggests that the tumors arise in the sheath of Schwann of the ciliary nerves. This had not as yet been encountered in melanoma of the iris. (7 figures, 62 references.) Vito La Rocca.

Waubke, Hans. **Bilateral enucleation on account of metastatic carcinoma of the choroid after cancer of the breast.** Klin. Monatsbl. f. Angenh. **114**:530-534, 1949.

A breast tumor was removed and 10 months later one eye was removed because of carcinoma of the choroid. Five months later a secondary glaucoma made a similar operation necessary on the other side. The patient died of general carcinomatosis three months after the second enucleation. One third of carcinomatous metastases in the choroid are said to be bilateral. Secondary glaucoma usually occurs several months before death. Early X-ray treatment of the involved second eye is recommended.

Max Hirschfelder.

17

INJURIES

Amsler, M., and Huber, A. **Sympathetic dyshoria.** Ophthalmologica **117**: 202-206, April-May, 1949.

For a number of years the authors have been interested in the rate of appearance in and disappearance from the aqueous of intravenously injected fluorescein in man. They have devised a simple optical method of estimating the fluorescein concentration of the aqueous in situ. For practical purposes it is sufficient to observe the rate of appearance of fluorescein in the eye during the thirty minute period following the injection. The authors consider the results of this test to be an expression of the permeability of the blood-aqueous barrier in the ciliary body. Applying this permeability test to various ocular conditions, they have noted a very interesting phenomenon which they now report under the name of "dyshorie sympathique" (δρος, boundary). This phenomenon consists of fluctuations in the permeability of the blood-aqueous barrier of the clinically normal eye that closely parallel fluctuations of ciliary permeability which occur in the other eye after a perforating injury. The fluctuations in permeability in the clinically normal eye occur, as a rule, within what Amsler and Huber consider the normal range of permeability. Eleven out of 56 patients whose one eye had sustained a perforating injury showed parallel fluctuations in the ciliary permeability of the clinically normal mate. The phenomenon does not occur in patients with unilateral endogenous uveitis. It is not an early symptom of sympathetic ophthalmia. It usually disappears without any serious developments in the uninjured eye.

Peter C. Kronfeld.

Braga de Amilhães, and Gomes da Silva. **Perforating injury of cornea by fishhook.** Arq. brasil. de oftal. **12**:55-61, 1949.

A young man of 19 years was hit in the right eye by a companion's fishhook. The cornea was pierced and a large hyphema produced, but without hurt to iris, ciliary body, or lens. Repair was undertaken about four hours after the accident, with use of sliding conjunctival flaps. Systemic treatment included six million penicillin units intramuscularly. Visual acuity on leaving hospital was 6/10. (3 figures.)

W. H. Crisp.

Perez Toril, F. **Ocular trauma.** Arch. Soc. oftal. hispano-am. **9**:534-536, May, 1949.

The frequency of serpiginous ulcers in the agricultural region is ascribed to the ignorance and poverty of the population, and to the prevalence of dacryocystitis, which is left untreated, until an insignificant corneal injury is converted into a grave infection. The author urges the use of mild antiseptics after trauma, education in sanitation, the use of protective goggles, and prompt medical assistance if the eye remains painful.

Ray K. Daily.

18

SYSTEMIC DISEASE AND PARASITES

Adler, F. H., Scheie, H. G., and Dennis, R. **Thyrotropic exophthalmos from**

the viewpoint of the ophthalmologist. J. Mich. St. M. Soc. **48**:852-857, July, 1949.

The authors discuss the differential diagnosis and the therapy of the two types of exophthalmos pathology associated with Graves' disease. The classical symptomatology and eye signs of diffuse toxic goiter, associated with high basal metabolic rate, are described. The eye findings are attributed to spasm of the smooth musculature of the orbit. The exophthalmos is only moderate, and edema of the lids and oculomotor palsies are infrequent. In thyrotropic exophthalmos, similar symptoms may be present, but the exophthalmos is marked, progressive, and often asymmetrical. The majority of these patients also show lid and conjunctival edema, all associated with histologic changes in the orbital musculature. These changes may occur without relation to elevated basal metabolic levels. They result from an excess of thyrotropic hormone of the anterior pituitary. Thyroidectomy is contraindicated as it removes the inhibitory control of the thyrotropic pituitary factor. Thyroid extract and iodine are used in the treatment of thyrotropic exophthalmos, and the authors have used irradiation of the pituitary, as well as estrogenic compounds. Orbital decompression operations are used when the visual function is threatened by the exophthalmos. Fourteen illustrative case reports are presented. Benjamin Milder.

Aznarez García, José. **Amaurosis and hysterical amblyopia.** Arch. Soc. oftal. hispano-am. **9**:648-665, June, 1949.

This is a very picturesque presentation of the subject and an account of seven cases of hysterical amblyopia, attributed to emotional conflicts arising from domestic difficulties, desire to escape military service, and feelings of guilt. All patients had complete amaurosis, in six it was bilateral, three patients were women and all were past the second decade of life, although it is more generally believed that unilateral amblyopia is more frequent in hysteria than amaurosis, and that most patients are women in the second decade of life. The author questions Charlin's statement that there is an interval between the psychic trauma and the onset of hysterical amaurosis.

The treatment described might be regarded as psychiatric heresy but was always successful in the author's hands; it consisted of binocular bandage, brief confinement in bed, pretended electrotherapy, and innocuous injections into the preauricular region. The suggestive effect of the injections was augumented in the days of German power by the information that the drug came from Germany; it is amusingly suggested that now their origin be attributed to North America. Ray K. Daily.

Cohen, M. **Ocular findings in three hundred and twenty-three patients with schizophrenia.** Arch. Ophth. **41**:697-700, June, 1949.

Of 323 patients with schizophrenia 31 percent had discs of normal color, 26 percent had a pronounced brown-gray discoloration of the temporal portion of the disc, and in 43 percent the discoloration was diffuse or complete. The ophthalmologic manifestations and clinical findings suggest the probable existence of a pathologic process affecting the visual pathway in schizophrenic patients.

John C. Long.

Curtis, A. C., Cawley, E. P., and Johnwick, E. B. **Association of progressive (malignant) exophthalmos and localized myxedema.** Arch. Derm. and Syph. **60**: 318-337, Sept., 1949.

Progressive exophthalmos is a more severe type of toxic diffuse goiter and not a separate entity. The thyroid-stimulating hormone of the anterior pituitary gland

causes glandular hyperplasia and increased metabolic rate, but with the development of an antihormone by the thyroid gland and after inactivation of the stimulating hormone by thyroxine, the thyroid gland becomes refractory and exophthalmos develops. If a large portion of the thyroid cells are removed by surgery, or if the cells of the thyroid gland can not respond to the stimulus, most of the thyroid-stimulating hormone remains active and progressive exophthalmos develops. Similarly the production of localized myxedema, of bilateral, oval, indurated, yellowish-brown pigskin-like plaques, can be attributed to an excess of the thyroid-stimulating hormone limited to the anterior surface of the legs. Localized myxedema is always associated with toxic diffuse goiter and thyroidectomy and thiouracil therapy usually initiates their onset. Eight case histories illustrate the authors' contention that progressive exophthalmos and localized myxedema are allied manifestations of the same underlying disorder, namely of an excess of thyroid-stimulating hormone.

R. Grunfeld.

Elliott, D. C. **Leprosy, a disease of childhood; with special reference to early findings in eye, ear, nose and throat of children examined at the National Leprosarium at Carville, La.** J. Pediatrics **35**: 189-196, Aug., 1949.

The characteristic and diagnostic manifestations of leprosy in 14 children are described. Episcleritis, in the interpalpebral spaces, is seen in the eyes of the older children. A characteristic beading of the corneal nerves was seen in 13 of these children. It is usually bilateral, in the superior temporal quadrants, and indicates that the disease must be of at least 10 years' duration. In time, punctate keratitis develops in these areas, and after 15 to 20 years an interstitial keratitis. A limbal neovascularization was also noted, frequently with a large vessel along the superior temporal quadrant. The author also describes filaments arising from the iris surface, but no "pearls" of leprous iritis were found in the children. The visual acuity was normal. Two of the 14 showed patches of inactive choroiditis, but in the others the ocular fundus was normal. Leprosy could be eradicated within two generations if children were removed from a leprous environment at birth and if increasing familiarity with the signs of the disease in children could be achieved to aid in early recognition and treatment.

Benjamin Milder.

Ferrata, L., and Montanelli, M. **The etiology of recurrent uveitis with hypopyon.** Ann. di ottal. e clin. ocul. **75**:10-19, Jan., 1949.

Many patients with recurrent uveitis with hypopyon have chronic articular rheumatism, and the authors regard both as of the same etiology. They point out several interesting parallelisms: infectiousness, recurrence, complete remissions, sterile exudate, good systemic response to salicylates, negative blood cultures, and cutaneous manifestations such as furunculosis and erythema nodosum. They suggest that the recurrent attacks may be precipitated by a parallergic factor. Two cases are presented and the literature is briefly reviewed.

Harry K. Messenger.

Friedmann, Martin. **Thelaziasis of the conjunctiva.** Ophthalmologica **118**:193-204, Sept., 1949.

The author reports a case of infestation of the conjunctival sac with Thelazia Callipaeda or "oriental eye worm." The preferred habitat of this nematode in man as well as in animals is the lacrimal apparatus and the conjunctival sac. In the case reported 35 percent of the white blood cells were eosinophiles. The author

believes that the infection occurs through the digestive tract and that various molluscs may serve as intermediate hosts. Due reference is made to the fundamental work in this field done by American authors (Kofoid and assoc., Univ. California Pub. Zool. 41, 225, 1937, and Hosford and assoc., Arch. of Ophth. 27, 1165, 1942). Peter C. Kronfeld.

Gifford, B. L., and Krause, A. C. **Differential diagnosis of Boeck's sarcoidosis.** Arch. Ophth. **41**:667-696, June, 1949.

The many uncertainties in the establishment of a clinical diagnosis of Boeck's sarcoidosis are discussed. Sarcoidosis is chiefly confused, usually on the basis of incomplete evidence, with tuberculosis, and less often with Hodgkin's disease, syphilis, neoplasms, silicosis, leukemias, leprosy, and other forms of lymphoblastoma. Most important for a correct diagnosis are a good history, clinical evidence of disease simulating sarcoidosis, loss of cutaneous sensitivity to tuberculin, skin biopsy, lesions of the bone, characteristic cutaneous lesions, examination of the blood for albumin-globulin ratio, and ocular examination. The items are listed in the approximate order of their reliability.

Ten cases of sarcoidosis are reported in detail. Ocular disease was present in approximately one-third of the cases. The usual sequence of events was the appearance of conjunctivitis, followed by some degree of keratitis, and anterior uveitis that occurred with the conjunctivitis or keratitis, or later. Secondary glaucoma was not observed; complicated cataract was infrequent, and chorioretinitis was rare. Vision was excellent when the cornea remained clear even though anterior uveitis had been severe and active for many years. John C. Long.

Gordon, B. L. **Effects of diabetes on cataract and on vision.** Arch. Ophth. **41**:462-472, April, 1949.

The literature is reviewed. It is evident that the mechanism of diabetic cataract (as of non-diabetic cataract) has not been demonstrated. The fact that hyperglycemia may cause cataract in young subjects and will not affect older persons shows that other factors contribute to the formation of cataract. These other factors include glandular disturbances, vitamin deficiencies and unbalanced metabolism of the capsule or the aqueous. While the effect of diabetes on the adult lens has not been scientifically demonstrated, it has been shown that this condition exhibits a tendency to alter vision. An increase in the blood sugar is accompanied by myopia, a decrease is associated with hypermetropia. This decrease may change the refraction from 1 to 4 diopters. A change of 7 diopters has been reported. The refractive changes are temporary. John C. Long.

Locket, S. **Blindness associated with hemmorrhage.** Brit. J. Ophth. **33**:543-555, Sept., 1949.

Visual disturbance or even blindness during or immediately after massive hemorrhage which seldom lasts over an hour, and ends in complete recovery, is quite common. Blindness of a longer duration and in most cases associated with permanent damage to the vision several days or weeks after massive or repeated hemorrhage is a different clinical entity with a bad prognosis. The first picture is associated with a simple reduction in the blood volume and a drop in the blood pressure and the latter with reduction of hemoglobin and of plasma proteins. Three new cases and all the cases in the literature are described. Treatment consists of high protein intake and repeated transfusions but is very unsatisfactory. Morris Kaplan.

Nutt, A. B., Wright, T., Bowie, J. H., and Beattie, C. P. **Case of toxoplasmosis.** Brit. M. J. pp. 905-907, Oct. 22, 1949.

A case of toxoplasmosis is reported in a 4-year-old girl. The child's mother, father, older sister, and younger brother, were examined and were found free of any ocular or mental disease.

Donald T. Hughson.

Paufique, L., and Etienne, R. **The genital origin of certain ocular diseases in the female.** Arch. d'opht. **9**:157-175, 1949.

The authors discuss the role of the female genital tract in the pathogenesis of ocular infections and report 13 examples of such a relationship. They conclude that in the young woman the frequency of genital tuberculosis is high, whereas in the menopausal or post-menopausal woman the ordinary pyogenic foci are the more frequent genital tract invaders. The genital lesions in the 13 cases were inflammations of the adnexa such as pelviperitonitis, complicated fibromas, and ovarian cysts with necrobiosis, and the ocular lesions were various types of uveitis and keratitis. In many instances the genital focus was inactive and symptomless, but suppression of the focus generally resulted in complete healing of the ocular disease. The best results are obtained when the ocular lesion is fresh and the genital lesion the only focus. They conclude that a genital examination should be a part of the systemic survey in endogenous disease.

Phillips Thygeson.

Rabadán Fernández, Pedro. **Ocular changes in malaria.** Arch. soc. oftal. hispano-am. **9**:596-619, June, 1949.

Brief case reports of 62 cases and a discussion of the ocular complications of malaria are presented without adding anything new.

Ray K. Daily.

Sabin, A. B., and Feldman, H. A. **Chorioretinopathy associated with other evidence of cerebral damage in childhood; a syndrome of unknown etiology separable from congenital toxoplasmosis.** J. Pediatrics **35**:296-309, Sept., 1949.

The authors describe two new, more precise, tests for toxoplasmosis, a dye test and a complement fixation test. The antibodies apparently persist at high levels for two to five years. Sixty children and their mothers were studied clinically and with serologic tests for toxoplasmosis. Some of the patients showing chorioretinopathy and cerebral damage had high antibody titers in the dye and complement fixation tests; others had low titers. The mothers of children with high titers also showed strongly positive serologic evidence; in the low titer group the proportion of positives among the mothers resembled an average adult population. Those who had pathologic evidence of toxoplasmosis all had high titers. No diagnosis of toxoplasmosis is justifiable on clinical grounds alone; conclusive serologic proof is necessary. In the presence of a characteristic chorioretinitis associated with cerebral calcification in infancy a diagnosis of toxoplasmosis is correct is 90 percent; without calcification, in only 10 percent. Nineteen of the children showed chorioretinitis and cerebral symptoms, but no cerebral calcification or positive serologic findings. This syndrome, which must be differentiated from toxoplasmosis, is probably the result of defective development.

Benjamin Milder.

Strong, J. A. **Thyrotoxicosis with ophthalmoplegia, myopathy, Wolff-Parkinson-White syndrome and pericardial friction.** Lancet **1**:959, June 4, 1949.

A 40-year-old woman suffered simultaneously from four, comparatively rare diseases syndromes. She had 1. bilateral exophthalmic ophthalmoplegia which progressed after the thyrotoxis was apparently under control. 2. thyrotoxic myopathy of the left vocal cord, of the sternocleidomastoid muscles, muscles of de-

glutition, and facial muscles, muscles which are all of cranial innervation, (biopsy revealed edema of the muscles, a kind which is usually found in thyrotoxic myopathy). 3. Wolff-Parkinson-White syndrome, or paroxymal tachycardia, caused by a bundle-track block in which the electrocardiogram marks a short P-R interval, a syndrome which has never been associated previously with thyrotoxicosis, and 4. precordial friction, a superficial friction rub heard mostly over the pulmonary base and probably produced mechanically. Treatment with methyl-thiouracil releaved the cardiac complication, but the eye signs and the myopathy persisted, suggesting that the latter symptoms are of thyrotropic origin. Injection of neostigmin temporarily increased the weakness of the muscles.

R. Grunfeld.

Zondek, H., and Lezynsky. **Retinitis pigmentosa and diabetes insipidus.** Sem. Hop. Paris **25**:2476-2478, Aug. 6, 1949.

A virtually blind 20-year-old woman who had retinitis pigmentosa since childhood also had idiopathic diabetes insipidus during the last four years, characterized by primary polydipsia and secondary polyuria. The patient exhibited no signs of such disease processes, as hypophyseal tumor, basal or posterior cranial tumor, inflammatory tuberculous or syphilitic meningitis, which are generally associated with true or essential diabetes insipidus, a disease of the anterior pituitary gland. The kidneys were not damaged; they could well eliminate concentrated urine of sodium chloride, bicarbonate, and other basic elements. The disease process was rather of psychic origin, of an increased thirst sensation. The thirst is regulated in the hypothalamic region subordinated to the cortex. Zondek had previously shown that retinitis pigmentosa is an affection of diencephalic origin because of the faulty mechanism of carbohydrate metabolism, tendency of hypoglycemia and decalcification of the cranial bones. It is therefore suggested that the two disease processes have a common, hypothalamic, origin.

R. Grunfeld.

19

CONGENITAL DEFORMITIES, HEREDITY

Bird, A., and McEachern, D. **Leber's hereditary optic atrophy in a Canadian family.** Canad. M. A. J. **61**:376-382, Oct., 1949.

A Canadian family with hereditary optic atrophy (Leber's disease) is described. The family was investigated to the sixth generation.

Donald T. Hughson.

Brégeat, P., and Naud, G. **A new case of mandibulo-facial dysostosis (syndrome of Franceschetti).** Arch. d'opht. **9**:427-440, 1949.

Brégeat and Naud describe the Franceschetti syndrome of mandibulo-facial dysostosis in a boy of 11 years. The essential lesions of the syndrome as observed in this case consisted of malformations of the lids with irregular implantation of the cilia, malformation of the orbit with hypoplasia of the malar bone, abnormal ear lobes, hypoplasia of the mandible, partial atrophy of the palatine bone, and antimongoloid obliquity of the palpebral fissures. In addition, the child had mild oxycephaly, spina bifida occulta, undescended testicles, partial syndactyly of the second and third toes, more marked on the right, and a severe hearing defect, especially on the right. The child lacked the blind fistulas between the mouth and middle ears and the irregular implantation of the teeth which were mentioned in Franceschetti's original description of the syndrome in 1944.

The authors discuss the embryological relationships of the syndrome and the

differential points between it and other groups of congenital malformations.

Phillips Thygeson.

Brooks, W. D. W., Heasman, M. A., and Lovell, R. R. H. **Retinitis pigmentosa associated with cystinuria; two uncommon inherited conditions occurring in a family.** Lancet **1**:1096-1098, June 25, 1949.

A 40-year-old woman had two inherited diseases, retinitis pigmentosa and cystinuria. Both have autosomal recessive character, but the gene for cystinuria was probably located on a different chromosome pair from that of the retinitis pigmentosa.

R. Grunfeld.

Cordes, F. C. **Cataract formation in the human embryo after rubella.** Arch. Ophth. **42**:596-605, Nov., 1949.

The changes in the eyes of an 11-weeks-old embryo are described. The mother had rubella during the latter part of the second month of pregnancy. Both eyes of the embryo showed cataract formation. In addition, the findings in three other embryos without cataract are reported. A review of the literature and an examination of five specimens from mothers who had rubella during the first three months of pregnancy bear out the clinical finding that cataract formation is seen in a definite percentage of such offspring. However, rubella contracted during the first trimester does not always result in changes in the lens.

Ralph W. Danielson.

Corrado, A., and Toselli, C. **The ocular complications of brucellosis.** Rassegna ital. d'ottal. **18**:163-170, May-June, 1949.

The authors review the literature and point out that all parts of the eye, as well as the brain and other organs, may be damaged by the brucella organism. Two cases are reported. In the first, the right eye of a 43-year-old woman developed herpetic keratitis with a mild iridocyclitis. Treatment consisted of atropine and antiseptics locally, brucella vaccine and injections of vitamine B_1. Recovery was satisfactory with vision of 7/10. The second case appeared in a 55-year-old man who had suffered from brucellosis for two years. The ocular complications consisted of lacrymal stricture, blepharoconjunctivitis and complicated anterior cortical cataract with pigment deposits. The treatment was not recorded.

Eugene M. Blake.

Falls, H. F., and Cotterman, C. W. **Choroidoretinal degeneration: a sex-linked form in which heterozygous women exhibit a tapetal-like retinal reflex.** Arch. Ophth. **40**:685-703, Dec., 1948.

A family was observed in which some of the males presented the appearance of typical retinitis pigmentosa while some of the females showed a structure resembling the tapetum lucidum of certain mammals. A pedigree is presented showing 105 relatives, of whom 75 were subjected to ophthalmoscopic examination. The distribution of cases of retinitis pigmentosa and tapetal reflex in the pedigree suggests the presence of a sex-linked gene producing both abnormalities. The affected males are in all cases the sons of mothers having the tapetal trait. On the assumption of a sex-linked factor which produces retinitis pigmentosa in males and the tapetum-like fundus in heterozygous females, we should expect equal numbers of affected and normal children among both sons and daughters of women showing the tapetal trait. Among children of affected males, however, all daughters, but no sons, would be expected to be affected. The observed frequencies are in obvious agreement with these expectations. All of those examined in this series except the young children were tested for defects in color vision. Such defects were found in two

sisters with the tapetum-like fundi and their father. John C. Long.

Kiskadden, W. S., McDowell, A. J., and Keiser, T. **Results of early treatment of congenital anophthalmos.** Plastic and Reconstr. Surg. **4**:426-433, Sept., 1949.

Congenital anophthalmos and extreme microphthalmos offer the same practical problems of treatment. The eyelids are usually normal except for their small size and concave contour. Usually the cilia, puncta, lacrymal gland and Meibomian glands are normal. The palpebral fissure is shortened. In some cases, the diminution in size of the socket and palpebral fissure may be below 50 percent; in traumatic anophthalmos, the relative size of the socket may be larger, but the loss of lining and lid tissue with scar formation and deformity of the bony orbit may present a problem quite similar to that of congenital anophthalmos. The conventional approach to this problem has been to enlarge the socket and palpebral fissure by dissection with the addition of lining in the form of skin or mucous membrane grafts.

A case of congenital unilateral anophthalmos treated in this manner is shown and the defects of this method are apparent. The palpebral fissure was lengthened to facilitate grafting, and the excess length required a later operation; also it remained lower than that of the fellow eye. The lids are thicker than normal, the margins are irregular, and there are no lashes in the lateral two-thirds.

Four cases corrected by progressive dilatation of the anophthalmic orbit are presented. The most important requirement for success is the opportunity to begin treatment in early infancy. The forms are not fitted from impressions, but instead, a wax form of the desired shape is fitted by trial until the maximum size that can be retained is reached. This is then duplicated in acrylic and inserted. Usually within a few days, a form nearly twice as large can be fitted. It is evident that the necessary increase in size of the socket can be most readily accomplished when dilatation is begun during the rapid growth of infancy when the bony and soft tissue is more mobile and adaptable. The popular idea of waiting until the patient is old enough to coöperate does not serve his best interests. By producing a most natural appearance and avoiding the disadvantages of surgery, this appears to be the treatment of choice. Eight photographs show patients and acrylic forms used. Alston Callahan.

Loddoni, J., and Duc, C. **A case of bilateral congenital anophthalmus.** Ann. d'ocul. **182**:774-775, Oct., 1949.

A female infant without eyes is described. Chas. A. Bahn.

Musini, Attilio. **The hereditary transmission of bilateral congenital blepharoptosis.** Ann. di ottal. e clin. ocul. **75**:45-54, Feb., 1949.

In three family trees presented by Musini the ptosis character shows monomeric dominance. From his studies of these trees Musini concludes that the ptosis character undergoes aggravation in successive generations, and that the presence of other characters (blepharophimosis, and particularly strabismus and epicanthus) normally associated with ptosis is an indication of greater severity. The most probable hypothesis is that these associated defects as well as the ptosis itself are due to the pleiotropic action of the same polyphenic gene. In all the affected persons who underwent operation the elevator muscle was found to be notably hypoplastic.

Harry K. Messenger.

Páez Allende, F., and Menchaca, F. **Bilateral congenital microphthalmos in an infant.** Arch. de oftal. d. Buenos Aires **23**:360-371, Nov.-Dec., 1948.

Microphthalmos is defined as an eye whose diameters are less than those of a normal globe. The author discusses various known factors such as the relative frequency, diagnostic appearance, embryology, possible etiology, pathologic anatomy and treatment. His description concerns the case of an eleven-months, probably blind girl with typical bilateral microphthalmos. He suggests, too, that a lack of vitamin A in the mother during gestation may be a causative factor. (4 figures, references.) Edward Saskin.

Pagliarani, N. **The problem of heredity in retinosis pigmentosa.** Boll. d'ocul. **28**: 339-348, June, 1949.

The author studied the familial factors in 156 cases of retinosis pigmentosa and related diseases, originating from 145 different families. Heredity was found in 42 families (29.9 percent) and consanguinity of the parents in 20 families (13.7 percent). In seven families, both heredity and consanguinity of parents was present. The type of heredity was recessive in 40, and dominant in 2 families. Of all patients, 98 were males, and 58 females, a relationship similar to that reported by Nettelship and Wilmer. Typical fundus pictures were found in 128 patients, unusual features in 28. Of these, 17 showed fundus changes involving mainly the posterior pole, 5 were "sine pigmento," two were complicated by macular colobomas, and one by questionable retinitis proliferans. In 28 patients the disease was congenital, in 75 infantile, in 44 juvenile, and in 9 it began in adult life. In 47 patients, the following complications were charted: high myopia in 15, deafness in 13, posterior cortical cataract in 8, other cataracts in 3, Lawrence-Moon-Biedl syndrome in 8, mental deterioration in 4, keratoconus in 3, glaucoma in 2, and coloboma of macula in 2. About 30 percent of all patients had one or more of these complications. The data do not support the assumption that different fundus pictures correspond to different types of hereditary transmission. (46 references.) K. W. Ascher.

Paul, T. O. **Blood groups and effects of roentgen irradiation in retrolental fibroplasia.** Arch. Ophth. **41**:659-666, June, 1949.

Retrolental fibroplasia was found in 4.4 percent of 223 premature babies who weighed less than 2,500 Gm. Of the 23 babies in the study who weighed less than 1,500 Gm., 7, or 30.4 percent, had the defect. Twelve cases are reported. Of 9 eyes treated with roentgen radiation, 3 showed slight thinning of the membrane at the less dense borders and 6 showed no apparent change. In no case was the thinning sufficient to be of any real help preliminary to needling of the lenses. Little or no effect on the vessels of the membrane could be observed. A study of the possibility that a blood factor is a cause of prematurity in this congenital malformation lead to no definite conclusion. The embryology and differential diagnosis of retrolental fibroplasia is discussed. John C. Long.

Saebø, Johan. **An investigation into the mode of heredity of congenital and juvenile cataracts.** Brit. J. Ophth. **33**:601-629, Oct., 1949.

The author reports pedigrees of 17 families with 27 cases of congenital or juvenile cataracts from an isolated county in Norway. In 9 families the parents were consanguineous and in 5 of these the parents were first cousins. The occurrence of senile cataracts in these families was of normal incidence. Anticipation was not found. In this small series the mode of inheritance was probably autosomal and recessive. No instance of dominant inheritance was observed.
Orwyn H. Ellis.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Berens, Conrad. **Research in ophthalmology and otolaryngology. The role of the American Academy of Ophthalmology and Otolaryngology.** Tr. Am. Acad. Ophth. pp. 5-17, Sept.-Oct., 1949.

The need for more and better organization, equipment, and staffing of more research laboratories and other facilities in our specialties is stressed. Among the few organizations mentioned which have reasonably modern and complete facilities are the Wilmer Institute, the New York Eye and Ear Hospital and George Washington University. Unfortunately, most medical colleges and hospitals have inadequate research facilities in Ophthalmology and Otolaryngology, and cannot or will not obtain them without endowments. Among the larger foundations which have been financially interested in this research are the Carnegie, Rockefeller, Ford and Kress, among the smaller foundations is the John and Mary Markle Foundation.

A national Institute for the Prevention of Blindness with adequate research facilities would cost approximately 15 million dollars to erect, equip and staff. This rather large amount would apparently more than justify itself within a reasonable time. Our Academy has made a considerable contribution to ophthalmic research both directly and indirectly over many years. At present, approximately $40,000 annually is donated by the Academy for projects involving research in ophthalmology and otolaryngology. More funds could be secured from industry for its sponsored projects. Modern research methods and their statistical evaluation may now be better understood through books, periodicals and professional aid. The practicing ophthalmologist and otolaryngologist can in many ways aid in important research through adequate records and greater interest in this subject. The many fields in which research is badly needed are illustrated by approximately 40 ophthalmic and otolaryngological topics suggested for investigation.

Chas. A. Bahn.

Bixler, D. P. **The establishment of an industrial vision program.** Tr. Am. Acad. Ophth. pp. 91-99, Sept.-Oct., 1949.

The following program was installed in a West Coast shipyard with approximately 8,000 workers. All employees were examined by screening methods and new visual requirements were established. Correcting lenses, safety goggles and other protective devices were used if necessary. Examination equipment was moved from shop to shop in a trailer to reduce lost time. Some of the refractive problems involved are discussed at length. Repairs and replacements of broken parts were handled at the safety equipment issue room. Of the first 4000 men examined 52 percent required and received visual care. A statistical table is presented to illustrate the number of refractions, goggles and other devices used.

Chas. A. Bahn.

Dolcet Buxeres, Luis. **Ocular diseases in the Spanish possessions on the Gulf of Guinea.** Arch. Soc. oftal. hispano-am. 9:525-531, May, 1949.

The observations made on a trip are reported in the hope of interesting young ophthalmologists in practicing in the area. At present there are no ophthalmologists there and the burden of ophthalmological service falls on the general practitioners. The native population has more confidence in their own medicine men than in the Spanish physicians, whom they consult as a last resort. Most injured eyes are seen too late for effective therapy. The most frequent ocular complications

of tropical diseases are those of tripanosomiasis, leprosy, and malaria. To see the ocular lesions caused by leprosy one has to visit the leprosaria in the interior. The natives are immune to malaria, which is seen only in Europeans; the most common ocular complication is the yellow discoloration of the skin and conjunctiva, caused by antimalarial drugs. Tuberculosis and syphilis are common, and miliary tuberculosis of the choroid is seen frequently. The most frequent parasitic diseases are filariasis and euliasis. There is no interest in refraction, except for the correction of presbyopia which sets in earlier than normal in the tropics even in Europeans. Cataracts are frequent and begin at about 40 years of age. Glaucoma was not encountered. Malignant tumors are seen at the stage when therapy is useless.

Ray K. Daily.

Gesell, Arnold. **The developmental aspect of child vision.** J. Pediatrics. **35**:310-316, Sept., 1949.

The author discusses the development of the visual function in children. A broad series of observations on children from premature infants to the age of ten years made clear that the complexities of the phenomenon of visual perception demand that we look at a child's visual performance as the resultant of an integration of various skills of the whole child. A full-term infant has an intrinsic visual achievement superior to that of a premature infant. The fixation response to an object involves some suppression of other activities, indicating that the entire action system is involved. Organization of the visual process involves development of three components: skeletal (ocular fixation), visceral (focussing), and cortical (interpretive). These components develop jointly, but not uniformly, each showing its own developmental gradient. Thus, there can be an almost infinite number of possible degrees of visual achievement in any given infant. The concept of the developmental mechanism is a factor to consider in evaluating the child who presents visual problems. The approach to study of the child's problem is all too frequently colored by our thinking in terms of adult visual mechanisms. In infancy, excessive hand regard or faulty postural orientation may suggest ocular dysfunction. Atypical motor patterns may be the result of birth trauma. In preschool years, various emotional and behavior problems may be due, basically, to visual difficulties. In the school years, the handling of children en masse tends to make unreasonable demands on some children. A more flexible educational approach may provide a more basic solution to the ocular problems of children than the use of therapeutic devices such as spectacles.

Benjamin Milder.

Haas, Emile. **The French Committee on Optics and its 1948 progress report.** Arch. d'opht. **9**:301-310, 1949.

The Comité français de l'optique was organized in 1948 to further the progress of the optical sciences and to assure the representation of French optical workers in the International Commission on Optics. Representatives from the major ophthalmologic societies of France included the doctors Bonamour, Haas, Onfray, and Polack. During the year the Committee produced a number of monographic reports on various optical subjects and completed an important bibliographic compilation. Haas reviews and analyzes the studies considered by the Committee which were of special ophthalmologic interest. Among the titles considered were the following: "Properties of glasses in relation to their structure," "Teaching of Microscopy," "Anatomogeometric constants of the eye," and "Treatment of optical surfaces. Reflecting and antireflecting layers." Haas called the

attention of French optical engineers to the pressing need for the development of new instruments for ophthalmologic use.

Phillips Thygeson.

Morgan, W. G., and Stump, N. F. **Benefits from professional eye care for workers with lowered visual performance.** Tr. Am. Acad. Opth. pp. 99-105, Sept.-Oct., 1949.

A visual survey of employees in the Owensboro Tube Works demonstrated that 39 percent were below visual requirements for their jobs. A direct relationship apparently existed between visual performance and average hourly piece work earnings. In many cases professional care resulted in greater earnings. In some instances employees were transferred to jobs which were better adapted to their visual qualifications. A visual survey on all new employees and periodic surveys of all employees are advised.

Chas. A. Bahn.

Nale, T. W. **Standing orders for traumatic cases in industrial dispensaries: eye accidents and injuries.** Tr. Am. Acad. Ophth. pp. 88-91, Sept.-Oct., 1949.

The usual first aid methods of diagnosis and treatment are outlined. Foreign bodies entering the eyes, traumatic injuries, flash and thermal burns, burns with hot metal and chemical or irritating fume burns must be treated at the scene of accident. Superficial foreign bodies in the eye, foreign bodies impacted in the cornea, corneal abrasions, corneal burns by hot scale, flash burns, penetrating foreign bodies and punctured wounds, contusions to the eye, thermal burns, chemical burns, delayed chemical burns and chemical fumes must be treated at the medical dispensary.

Chas. A. Bahn.

Piesbergen, Hermann. **A system for eye diseases.** Klin. Monatsbl. f. Augenh. **115**:1-12, 1949.

In customary ophthalmic nomenclature ophthalmic diseases are subdivided according to etiology, or according to function, or anatomical or ophthalmoscopical findings. The author proposes a system which names the actual pathologic process in the nomenclature of general pathology. Groups of similar diseases based on the same pathologic factor are established within this system. An etiologic diagnosis may be added and different stages of disease may have subsidiary names. The author emphasizes the use of the word "retinopathy" for degenerative retinal disease, proposes the term "retinosis edematosa" instead of "retinitis albuminurica," uses the word "closure of the artery or vein" instead of embolism or thrombosis and coins the term "retinosis neuroepithelialis" for retinitis pigmentosa. Primary ocular diseases frequently lead secondarily to a multitude of other conditions and subdivision into primary and secondary pathologic processes is indicated.

Max Hirschfelder.

Podesta, H. **The manner of seeing and painting in color blind artists.** Klin. Monatsbl. f. Augenh. **114**:401-412, 1949.

The color blind German artist Wilhelm von Kuegelgen (1802-1867) described his difficulties in his autobiography. He was frequently aided by his wife in the judging of colors. He was red-green blind. Green appeared as a "reddish-brown" to him but the defect did not prevent him from turning out paintings which found wide acclaim.

Max Hirschfelder.

Runge, P. M. **A method of preservation of animal eyes.** Arch. Ophth. **40**:704-706, Dec., 1948.

The value of animal eyes in the teaching of surgical technique makes some means of preservation most desirable. Enucleated animal eyes may be kept indefinitely by freezing them in Locke's

solution as ice cubes in the ordinary refrigerator. The freezing process takes approximately one hour. The individual cubes may be wrapped in waxed paper and stored in the refrigerator or in a "deep freeze." The frozen eyes may be transported if packed with carbon dioxide snow. John C. Long.

Salzmann, Maximilian. **Oguchi's disease.** Ophthalmologica **118**:145-148, Sept., 1949.

On the occasion of J. Meller's seventy-fifth birthday Salzmann reminisces about a patient whom he saw in 1892, complaining of night-blindness and exhibiting "a peculiar, never-before-described and unexplainable" appearance of his eye grounds which 15 years later was recognized and reported by Oguchi as a new disease entity.

Peter C. Kronfeld.

Spyratos, S. **Hemeralopia and other ocular changes due to famine in Greece from 1941 to 1945.** Ann. d'ocul. **182**:672-685, Sept., 1949.

Anasarca, as well as edema of the orbital and ocular structures, was observed during the famine in Greece during 1941 and 1942. Various inflammatory and degenerative ocular changes occurred with the edema. In 1944 the incidence of hemeralopia was greatly increased. This was five times more frequent in males and occurred most often between the ages of 15 and 24 years. Degenerative changes in the pigment epithelium of the retina associated with disturbances of lipid and vitamin A metabolism were the underlying causes of the hemeralopia. Various irregular contractions of the peripheral fields were observed. Chas. A. Bahn.

Walker, G. L. **Retinopathy in the young diabetic.** J. Iowa St. M. Soc. **39**:384-386, Aug., 1949.

Diabetic retinopathy occurs in 76 percent of patients less than 30 years of age who have had diabetes for more than 10 years. The vascular damage occurs on the venous side of the circulation, starting with a venous stasis. The red dots are micro-aneurysms in the inner nuclear layer and are between the arterial and venous precapillaries. Aneurysms are due to weakening of the vessel walls and increased pressure. Rutin seems to help in 25 percent of the cases. I. E. Gaynon.

PAN-AMERICAN NOTES

Edited by Manuel Uribe Troncoso, M.D.
500 West End Avenue, New York 24

Communications should reach the editor by the 12th of the month

Mexico

Histopathology course given

Dr. Brittain Ford Payne gave a course on the "Histopathology of the Eye" in Mexico City under the auspices of the Mexican Ophthalmological Society. The course on histology was given from August 15th to 19th and included histology and detailed microscopic anatomy of the different membranes from the cornea to the retina and optic nerve. The course on pathology was given from August 22nd to 26th and included diseases of the cornea, sclera, and anterior segment of the eye.

New library of the Mexican Society

On August 26, 1949, under the presidency of Dr. Martinez Hinojosa, the new library was opened in the presence of the Secretary of Public Education and the Secretary of Health and Welfare of Mexico and other guests. A plaque was affixed to the entrance of the library in recognition of the benefactors of the library. The opening message was read by Dr. Martinez Hinojosa in the absence of Dr. Manuel Uribe Troncoso, honorary president of the society. Dr. Brittain Ford Payne closed his course on "Histopathology of the Eye," and the students received certificates of attendance. The ceremony ended with the showing of a film made by Professor Filatov on "Corneal grafts" lent by the Russian Embassy in Mexico City.

Archivos de la asociacion para evitar la ceguera en mexico

This is volume six of the series of the Reports of the Society for the Prevention of Blindness in Mexico and contains the proceedings of the meetings for the year 1948. It is a large volume consisting of 387 pages, with papers by 16 Mexican authors and eight foreign ophthalmologists. The president, Dr. L. Sanchez Bulnes, and the secretary, Dr. Daniel Silva, as well as the other members of the association, are to be congratulated on the contents of this splendid publication, which reflects the interest of Mexican ophthalmologists in questions pertaining to the conservation of vision. The papers are preceded by a statistical account of the work done at the association's hospital during 1947.

Among the most interesting papers are: "The role of illumination in the prevention of blindness," Dr. Daniel Silva; "The spherical equivalent in cross-cylinder tests," Dr. Joseph I. Pascal; "Penetrating wounds of the eyeball, intraocular foreign bodies, sympathetic ophthalmia," Dr. L. Vergara Espino, Dr. Armando Ramirez, and Dr. F. Arenas Bolaños; "Routine examination and treatment in concomitant motor anomalies," Dr. Teodulo Agundis; "Synkinetic superaction of the inferior oblique," Dr. George P. Guibor; "Record of the incidents and accidents occurring in 166 cases of cataract operations," Dr. Luis Sanchez Bulnes; "Useful hints for the extraction of cataracts," Dr. Ray K. Daily and Dr. Louis Daily, Jr.; "New statistical data on ocular onchocercosis," Dr. M. Puig Solanes; "Radiological exploration of the lacrimal passages in patients operated for dacryocystorinostomisis," Dr. Ramon Olivera Lopez; "A case of Spielmeyer-Vogt syndrome," Dr. Teodulo Agundis, Jr.; and "Iontophoresis in intraocular infections," Dr. M. P. Palmer.

Brazil

Arquivos do instituto penido burnier

This large volume (VIII) includes the Proceedings of the Ophthalmological Department of the Institute which is now functioning in its new building. Following are some of the papers listed: "Ocular cysticercosis," Dr. Lech, Jr.; "Laurence-Moon-Bardet-Biedl syndrome," Dr. J. Penido Burnier; "Keratoconus and persistence of the thymus," Dr. A. Almeida; "Congenital cataract consecutive to German measles during pregnancy," Dr. J. Penido Burnier and Dr. L. Souza Queiroz; "Nasal rhinosporidiosis," Dr. M. Alfonso Ferreira Filho and Dr. F. J. Monteiro Sales; "Contributions to tonometry," Dr. Penido Burnier Filho; and "Megaloleproma of the cornea," Dr. Linneu Silva.

The book ends with the Reports of the Meetings of the Society from 1945 to 1948.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received by the editor at least three months before the date of occurrence.

MISCELLANEOUS

ABSTRACTORS WANTED

The JOURNAL is in need of an abstractor to review the current Greek literature as well as one or two abstractors for Italian periodicals. For further information, please communicate with the abstract editor, Dr. F. Herbert Haessler, 561 North 15th Street, Milwaukee 3, Wisconsin.

ANNOUNCEMENTS

AMERICAN BOARD EXAMINATIONS

Candidates for the certificate of the American Board of Ophthalmology are accepted for examination on the evidence of a written qualifying test. These tests are held annually in various parts of the United States. Applications are now being accepted for the 1951 written test. They will be considered in order of receipt until the quota is filled.

Practical examinations for acceptable candidates for 1950 will be held in Boston, May 22nd to 26th; in Chicago, October 2nd to 6th; on the west coast in January, 1951.

NEW DIRECTORY OF DIPLOMATES

A new directory of diplomates of the American Board of Ophthalmology will be published shortly. No biographical material will be included. Diplomates are urged to keep the board's executive office, 56 Ivie Road, Cape Cottage, Maine, informed of changes of address at all times.

OREGON ACADEMY ANNOUNCED

The annual spring convention in ophthalmology and otolaryngology will be held in Portland, March 19th to 24th. This year the meeting has been divided into two sections: (1) Otolaryngology, which will be held Monday, Tuesday, and Wednesday morning; (2) Ophthalmology, which will be held Wednesday afternoon, Thursday and Friday morning.

Among the guest speakers will be Dr. John R. Lindsay, professor of otolaryngology, The University of Chicago Medical School; Dr. Gordon D. Hoople, professor of otolaryngology, Syracuse University Medical School; Dr. Paul Chandler, professor of ophthalmology, Harvard University Medical School; Dr. Michael J. Hogan, associate professor of ophthalmology, The University of California Medical School.

On Thursday evening, March 23rd, Dr. Paul Chandler will deliver the first John E. Weeks Memorial Lecture in Ophthalmology. On Friday afternoon and evening, the annual meeting of The Pacific Coast Section of the Association for Research in Ophthalmology will be held.

For further information, please communicate with Dr. David DeWeese, secretary, 1216 S.W. Yamhill Street, Portland 5, Oregon.

COURSE AT TULANE UNIVERSITY

The Department of Ophthalmology and the Division of Graduate Medicine, Tulane University, New Orleans, will conduct a continuation course in ophthalmology in New Orleans, March 13th to 18th.

Guest lecturers will be: Dr. Daniel B. Kirby, New York, New York, professor emeritus of ophthalmology, New York University Medical School; Dr. Frank B. Walsh, Baltimore, Maryland, associate professor of ophthalmology, Johns Hopkins University and Wilmer Eye Institute; Dr. Robert J. Masters, Indianapolis, Indiana, professor of ophthalmology, University of Indiana Medical School; Dr. Harold Falls, Ann Arbor, Michigan, associate professor of ophthalmology, University of Michigan Medical School; and Dr. Charles Sheard, distinguished lecturer in ophthalmology, Tulane University of Louisiana, professor emeritus of experimental biophysics, Graduate School, University of Minnesota (Mayo Clinic). Additional lectures will be given by resident faculty members of the Department of Ophthalmology, Tulane University.

SOCIETIES

AMERICAS UNITE TO SAVE SIGHT

A midcentury conference on progress in the prevention of blindness will be held March 26th to 31st by the National Society for the Prevention of Blindness and the Pan-American Association of Ophthalmology at the Floridian Hotel, Miami Beach, Florida.

SUNDAY, MARCH 26, 1950

1:00 p.m. Registration and viewing exhibits
5:00 p.m. Reception
Evening Free

MONDAY, MARCH 27, 1950

8:00 a.m. Registration
9:00 to 12:00 (noon) General Assembly:
Presiding: Conrad Berens, president, Pan-American Association of Ophthalmology;
Mr. Mason H. Bigelow, president, National Society for the Prevention of Blindness;
Dr. A. Vazquez Barriere, president, II Pan-American Congress, Montevideo, Uruguay;

Dr. Tomas R. Yanes, president, III Pan-American Congress, Havana, Cuba;
Dr. Antonio Torres Estrada, president, IV Pan-American Congress, Mexico City, Mexico;
Dr. Cesar de Andrade, president, National Council of Education, Rio de Janeiro, Brazil.
Welcome by *Honorable Harold Turk*, mayor, Miami Beach.

Intervention of the state in the battle against blindness. Dr. A. Vazquez Barriere, chairman, committee on the prevention of blindness of the Pan-American Association of Ophthalmology.

Testing visual fields by flicker fusion. Dr. Paul W. Miles, St. Louis, Missouri.

Rice diet for hypertension: Fundus photographic demonstration. Dr. W. B. Anderson and Dr. Walter Kempner, Duke University, Durham, North Carolina. Discussant: Dr. Frederico Cerboni, Buenos Aires, Argentina.

2:00 p.m. Presiding officers: Dr. A. Vazquez Barriere, Montevideo, Uruguay; Dr. John A. MacMillan, Montreal, Canada; Dr. Nelson M. Black, Miami, Florida.

Recent advances in ocular therapeutics. Dr. P. Robb McDonald, Philadelphia, Pennsylvania. Discussants: Dr. Paulina Satanowski, Buenos Aires, Argentina; Dr. John Bellows, Chicago, Illinois.

New opportunities in teaching ophthalmology. Committee on Teaching of Ophthalmology: Dr. Cecil S. O'Brien, Iowa City, Iowa; Dr. James H. Allen, Iowa City, Iowa; Dr. Alberto Urretz Zavalia, Cordoba, Argentina.

Preventing blindness in the Americas. Five-minute prevention of blindness reports from each of the American republics.

Legislation regarding the prevention of blindness. Dr. Hermino de Moraes Brito Conde, Rio de Janeiro, Brazil.

8:00 p.m.

Business meeting of the Pan-American Association of Ophthalmology.

8:30 p.m.

Preview of Mexico—1952. Color movies. Dr. Luis Sanchez Bulnes, Mexico, D.F.

Intraocular tumors (colored photographic demonstration). Mrs. Helenor Campbell Wilder, Armed Forces Institute of Pathology, Washington, D.C.

TUESDAY, MARCH 28, 1950

9:00 a.m. Presiding Officers: Dr. Bascom H. Palmer, Miami, Florida; Dr. Cesar de Andrade, Rio de Janeiro, Brazil.

Effects of excessive sunlight on the eyes: (a) At high altitudes, Dr. Jorge Valdeavellano, Lima, Peru; (b) At sea level, Dr. Robinson D. Harley and Dr. Robert Peckham, Atlantic City, New Jersey; (c) Visual effect of supersonic speed, Colonel Victor Byrnes, Randolph Field, Texas. Discussants: Dr. John L. Matthews, San Antonio, Texas; Dr. Brittain F. Payne, New York.

How good are contact lenses, Dr. Baudilio Courtis, chairman, Contact Lens Committee, Buenos Aires, Argentina. Discussants: Dr. Arno Town, New York; Dr. Daniel Silva, Mexico, D.F.

Symposium: Parasitic diseases. Moderator: Dr. M. Puig Solanes, Mexico; Dr. Rafael Pacheco Luna, Guatemala City; Dr. Nicolino Robello Machado, Santos, Brazil; Dr. Alson E. Braley, New York.

Hemispheric control of eye infections. Dr. Fred L. Soper, director for Western Hemisphere, World Health Organization, Pan-American Sanitary Bureau, Washington, D.C.

Nonpenetrating keratoplasty, Dr. Jorge Malbran, Buenos Aires, Argentina. Discussant: Dr. Ramon Castroviejo, New York.

2:00 p.m. Presiding Officers: Dr. Franklin M. Foote, Executive Director, National Society for the Prevention of Blindness; Dr. Luis Sanchez Bulnes, Director, Mexican Society for the Prevention of Blindness.

Teamwork for prevention (panel discussion). Discussants: Frank Woods, president, Illinois Society for the Prevention of Blindness, Chicago; Judge Ned H. Smith, president, Detroit Society for the Prevention of Blindness; Harry Simmons, executive director, Florida Council for the Blind, Tampa; Miss Anne E. Geddes, chief, statistics and analysis division, Federal Security Agency, Washington, D.C.; John L. Fortson, director of public relations, National Society for the Prevention of Blindness.

WEDNESDAY, MARCH 29, 1950

9:00 a.m. Presiding Officers: Dr. R. Bellido-Tagle, Lima, Peru; Dr. W. Y. Sayad, West Palm Beach, Florida.

Research in testing children's vision. Dr. Richard G. Scobee, St. Louis, Missouri.
Paper by Dr. Arnold Gesell.

Room A. Presiding Officer: Dr. Ricardo Fernandez, San Juan, Puerto Rico.

Round table on industrial eye problems. Dr. Albert C. Ruedemann, Detroit, Michigan. Dr. Lino Vergara Espino, Mexico City, Mexico, Safety Director, Florida Light & Power Co.; Personnel Director, Florida Light & Power Co.; John Scott, Jr., Rocky Mount Hills, Rocky Mount, N.C.

Room B. Presiding Officer: Dr. Shaler Richardson, Jacksonville, Florida.

Symposium on trachoma. Trachoma control in Argentina: Dr. Magin A. Diez, Buenos Aires, Argentina; Dr. Esteban Adrogue, Buenos Aires, Argentina; Dr. Virgilio C. Victoria, Tucuman, Argentina. Trachoma control in the United States: Dr. A. A. Siniscal, Rolla, Missouri; Dr. K. W. Cosgrove, Little Rock, Arkansas. Trachoma control in Brazil: Dr. Cesario de Andrade, Rio de Janeiro, Brazil. Progress in the treatment of trachoma in the past ten years, Dr. Penido Burnier, Campinas, Brazil.

2:00 p.m. Presiding Officers: Dr. Jorge Balza, Buenos Aires; Dr. Daniel B. Kirby, New York.

Recent advances in military ophthalmology. Dr. Cesar A. Rodriguez, Lima, Peru; Colonel Victor Byrnes, U. S. Air Forces; Dr. Feliciano Palomino Dena, Mexico City.

Visual acuity standards for: Military forces, Dr. Brittain Payne, New York; Civil Service personnel, Dr. Blackwell.

Symposium: Blindness in premature babies from retrolental fibroplasia. Moderator: Dr. Algernon B. Reese, New York. Dr. Parker Heath, Boston, Massachusetts; Dr. Arlington C. Krause, Chicago, Illinois; Dr. Arthur C. Unsworth, Hartford, Connecticut; Dr. William Turnbull, Montreal, Canada.

Eye diseases in infancy. Dr. Enrique Cipriani, Lima, Peru. Discussant: Dr. John A. MacMillan, Montreal, Canada.

THURSDAY, MARCH 30, 1950

9:00 a.m. Presiding Officers: Dr. Antonio Torres Estrada, Mexico City; Dr. Brittain Payne, New York City.

Transforming individuals through cosmetic and plastic surgery. Dr. Alston Callahan, Birmingham, Alabama. Discussants: Dr. Norman L. Cutler, Wilmington, Delaware; Dr. Pedro Garcia Nocito, Buenos Aires, Argentina; Dr. Otis S. Lee, Iowa City, Iowa.

Symposium: Secondary glaucoma. Moderator: Dr. F. Bruce Fralick, Ann Arbor, Michigan. Secondary to cataract, Dr. Ralph O. Rychener, Memphis, Tennessee; Secondary to uveitis, Dr. William B. Clark, New Orleans; Secondary to trauma, Dr. William S. Knighton, New York; Congenital glaucoma, Dr. Saul Sugar, Detroit, Michigan. Discussants: Dr. R. Bellido-Tagle, Lima, Peru; Dr. Raul Arganaraz, Buenos Aires, Argentina; Dr. Feliciano Palomino Dena, Mexico, D.F.; Dr. Enrique Graue, Mexico, D.F.

Provocative drinking tests as an indication for surgery in glaucoma. Dr. Santiago Barrenechea, Santiago, Chile. Discussants: Dr. Julio Raffo, Lima, Peru; Dr. Peter Kronfeld, Chicago.

Clinical use of D.F.P. in ophthalmology. Dr. Olga Ferrer, Havana, Cuba. Discussant: Dr. Charles Bahn, New Orleans, Louisiana.

2:00 p.m. Group discussion: *Protecting the eyes of the school child.*

Room A

Finding the child with eye defects. Leader: Richard G. Scobee, M.D., St. Louis. Discussants: Helen E. Weaver, R.N., New York; Frances E. M. Reed, M.D., Jacksonville; Mrs. Ben Humphries Gray, Chicago; Dr. Luis Sanchez Bulnes, Mexico City.

Room B

Lighting the classroom. Leader: Dr. Ray L. Hamon. Discussants: J. Fred Horn, Tallahassee; James E. Garland, Miami; A. C. Bergh, Miami.

Room C

The partially sighted child. Leader: Winifred Hathaway. Discussants, Marjorie A. C. Young, New York; Laura L. Sutter, Miami; Mrs. Ruby Norrell, Tampa; Mrs. Dorothea Payne, Miami; Mrs. Preston R. Yoakley, Tallahassee; Miss Louise Pickle, Tallahassee; Shaler Richardson, M.D., Jacksonville.

4:00 p.m. Summary of panel discussions.

FRIDAY MORNING, MARCH 31, 1950

Research program

1. *Hyaluronidase: An aid to local anesthesia in ophthalmology.* Harvey E. Thorpe, M.D.
2. *Manometria de la camara anterior del ojo.* Antonio Torres Estrada, M.D.
3. *Protein transport in ocular structures.* Albert M. Potts, Ph.D., M.D., Lorand V. Johnson, M.D., Mildred Orchen, and Doris Goodman.
4. *The effect of recommended human therapeutic doses of micro-wave diathermy on rabbit eyes.* William B. Clark, M.D., Bertha R. Noble, M.D., and Aleta Barbour, Ph.D.
5. *Esotropia: A statistical study.* R. G. Scobee, M.D.
6. *Studies of toxoplasma in tissue cultures.* T. Suie, Jr., M.Sc., Jackson W. Riddle, Ph.D., M.D., Arthur M. Culler, M.D.
7. *Effect of anticonvulsant drugs on retinal metabolism.* Anita P. Gilger, M.D., Albert M. Potts, Ph.D., M.D., Lorand V. Johnson, M.D.

PHILADELPHIA OFFICERS

Officers for the Section on Ophthalmology, College of Physicians of Philadelphia, are: Chairman, Dr. Wilfred E. Fry; clerk, Dr. M. Luther Kauffman. The meeting of the section is held at 8:15 p.m. the third Thursday of every month from October through April, at the College of Physicians Building.

AMERICAN BOARD OFFICERS

Officers of the American Board of Ophthalmology for 1950 are: Chairman, Dr. Algernon B. Reese; vice chairman, Dr. John H. Dunnington; secretary-treasurer, Dr. Edwin B. Dunphy.

PERSONALS

Emory University School of Medicine announces the promotion of Dr. F. Phinizy Calhoun, Jr., to professor and chairman of the Department of Ophthalmology; and Dr. Alton V. Hallum to professor of clinical ophthalmology.

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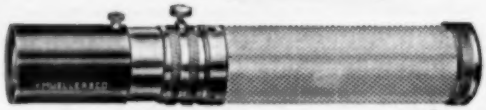

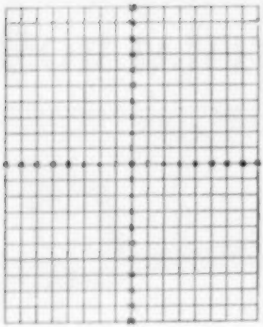

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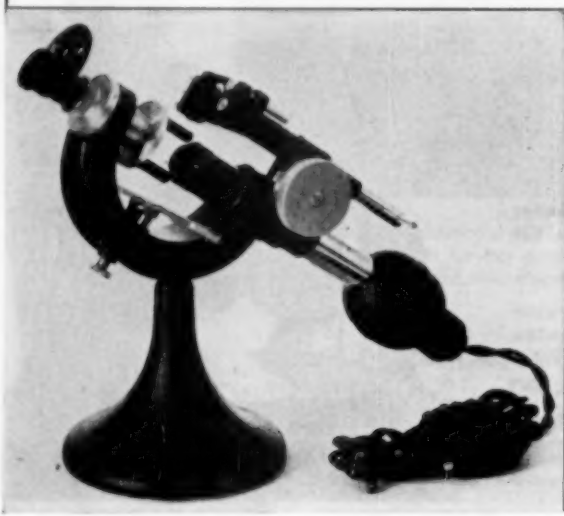

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Complete program and details will be mailed upon request addressed to Dr Howard H. Cummings, Chairman, Department of Postgraduate Medicine, University Hospital, Ann Arbor, Michigan.

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Five days—March 13 through 17, 1950
A continuation of Part I, with drills in making tests and examination of patients for diagnosis.

DIFFERENTIAL DIAGNOSIS WITH THE SLIT LAMP
Part time—9 a.m.-1 p.m.
February 27 through March 3, 1950
This course consists of diagnosis of diseases of the anterior segment of the eyeball and of the different mediums of the eye. Includes a thorough demonstration of the principles of illumination by means of the slit lamp.

EXTERNAL DISEASES OF THE EYE
Five days—2-5 p.m.
February 27 through March 3, 1950
Clinical differential diagnosis of types of conjunctivitis. Office procedures are demonstrated. The clinical types of bacterial, virus and allergic inflammations of the outer eye are presented with lectures, photographs, and clinical demonstrations.

OCULAR EXPRESSIONS OF SYSTEMIC DISEASE
Five days—9 a.m.-12 m.
February 27 through March 3, 1950
This course will cover eye changes associated with diabetes, hypertension and nephritis. It will also cover the changes of the eye associated with thyroid dysfunction and blood dyscrasias.

OPHTHALMIC NEUROLOGY (FOR SPECIALISTS)
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By

Austin Belgard

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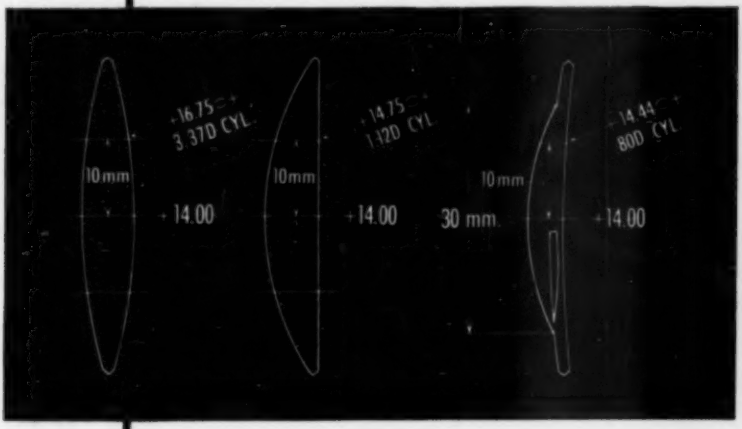

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